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Allergic Rhinitis

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Abstract

Instead of considering allergic rhinitis as a disease of acute symptoms, it needs to be understood as a chronic inflammatory disease that involves a level of persistent inflammation even in the absence of symptoms. Given the close functional, immunological and clinical link between asthma and rhinitis, it is reasonable to expect that an effective treatment of rhinitis would affect the co-morbid asthma; the occurrence of rhinitis in asthmatic patients ranges from 70% to about 90%. The prevalence of allergic rhinitis in patients presenting to their primary care providers with nasal symptoms is estimated to be 30% to 60%. Diagnostic allergy testing is indicated only if the test result could alter the decision to treat. Empirical treatment is a common approach, as allergic rhinitis is anonfatal disease with safe and effective treatments. Nonsedating antihistamines and nasal steroids are relatively free of side effects, and are reasonably inexpensive. The nasal steroids reduce all symptoms, but the antihistamines are less effective for nasal congestion and minimally address the problem of inflammation. Immune-based specifically targeted molecules, such as the cloned humanised monoclonal antibody-inhibiting human IgE omalizumab, are presently being studied in patients with seasonal allergic rhinitis.

Introduction

Accumulating evidence suggests that allergic rhinitis is a chronic inflammatory disease instead of a disease of acute symptoms. Therefore, even when symptoms are absent, a minimal level of inflammation may persist and the treatment strategy may need to include managing subclinical persistent inflammation.[1] If both inflammation and hyper-responsiveness can persist without symptoms, then symptoms can no longer be considered the unique markers of allergic disease.[2]

In fact, it has been shown that even when exposure to allergens is too low to provoke symptoms, there is still inflammatory infiltration in the nasal mucosa.[3] The underlying goal of treatment guidelines for allergic rhinitis is the effective treatment of symptoms, but this concept of minimal persistent inflammation suggests a different approach to therapy in which symptoms can be considered the "tip of the iceberg" of the allergic reaction with inflammation and hyper-responsiveness representing the submerged iceberg.[4]

There is compelling evidence that a link exists between the upper and lower respiratory tracts and that rhinitis has a remarkable impact on asthma. The inflammatory process which develops in the nose and bronchi explains some of the complex interactions between different clinical diseases such as rhinitis, sinusitis, asthma, bronchial hyper-responsiveness and viral infections.[5] This suggests some operative definitions: allergic Rhino-bronchitis[6], or United Airways Disease[7], or "one airway, one disease"[8] . The concept of CARAS (Combined Allergic Rhinitis and Asthma Syndrome) has important therapeutic implications.

The occurrence of rhinitis in asthmatic patients ranges from 70% to about 90%, when strict criteria are used. [9,10]

The respiratory tract is a single morpho-functional entity and is entirely covered by ciliate epithelium and mucinous glands down to the smallest bronchi. The limits imposed by the anatomical structures of nose and bronchi must be taken into account. The nose and paranasal sinuses are rigid boxes where erectile sinusoids predominate, whereas bronchi are included in elastic parenchyma and they are rich in smooth muscle tissue.

Therefore, β2 agonists can resolve asthma attacks but they have no effect on rhinitis. On the contrary, H_1 receptor antagonists treat rhinitis symptoms, but they are quite ineffective on broncho.constriction. However, a synergistic effect has been demonstrated for antihistamines in association with antileukotrienes. The association could reduce both rhinitis and asthma symptoms.

Prevalence

Allergic rhinitis (intermittent or persistent) must be distinguished from other forms of rhinitis, i.e. infectious, vasomotor, non-allergic rhinitis with eosinophilia syndrome (NARES), occupational, drug-induced, atrophic, and idiopathic.

Allergic rhinitis is the most common form of respiratory allergy, affecting 15 to 20% of the general population. However, until the age of four years, a clinical manifestation of IgE-mediated allergy in the ears, nose and throat is rare and the obvious expression of allergic rhinitis is not seen until after the age of four or five years.

The prevalence of allergic rhinitis is greatest during the teenage years and the early 20's and decreases thereafter.

In the elderly it is generally non-allergic mechanisms such as autonomic imbalance, an alteration in muscarinic receptors, or the sequelae of earlier nasal disorders and their treatment that are responsible. Allergic mechanisms are rarely the cause of perennial rhinitis. Nasal hyper-responsiveness in the elderly may manifest as "old mans drip", a clear profuse watery rhinorrhoea which forms a dewdrop at the end of the nose.

Mediators of symptoms

The classic allergic symptoms of sneezing, nasal obstruction, pruritis and rhinitis are produced by mediators preformed in mast cells and rapidly released (histamine, kinins), and by mediators newly generated from the arachidonic acid cascade when phos.pholipid membranes are disturbed (leukotrienes, prostaglandins, thromboxanes, eicosianoids). Late-phase reactions, beginning 3 to 5 hours after antigen exposure and peaking at 12 to 24 hours, are characterised by nasal congestion and hyper-reactivity caused by inflammator y cell accumulation at the site of the previous allergic reaction (allergen contact).[1] As early as two hours after allergen exposure, eosinophil levels significantly increase in nasal lavage fluids. Eosinophil activation and their levels are clearly essential to the allergic imflammation.[12] They release granules containing toxic basic proteins, the major part of which is represented by eosinophil cationic protein (ECP), which is measured in high levels in the nasal fluid of patients with different upper airway diseases.[13] The cysteinyl leukotrienes act through the Cys LT-receptor and are impor tant to the chemotoxis of eosinophils.[14] They have also been reported to increase the expression of histamine receptors on macrophages and smooth muscle cells, providing a mechanism for amplifying responses to histamine.[15]

Diagnosis

The prevalence of allergic rhinitis in patients presenting at primary care facilities is estimated to be 30% to 60%.[16] The disease probability is clinically significantly increased if the patient has been exposed to animal or pollen triggers, or has a previous history of allergy, or a family history of allergy.

The stereotypical signs and symptoms of allergic rhinitis are usually sufficient to arrive at the correct diagnosis. However, laboratory testing to confirm the clinical suspicion may be useful when symptoms are perennial instead of seasonal, or when patients do not respond favourably to standard treatment regimens. Skin tests (prick or intradermal) are relatively inexpensive while RAST, although expensive, is not influenced by the presence of antihistamines. As allergic rhinitis is a nonfatal disease with effective treat-ment, it may not be necessary to have absolute precise estimates of allergy test diagnostic performance. Diagnostic allergy testing is only indicated if the test result could alter the decision to treat.[16] When patients do not respond to medication and treatment must be increased to incorporate allergen avoidance and specific immunotherapy, it is important to know what the allergen is. In this setting, allergy testing guides treatment.

Untreated rhinitis symptoms may lead to inability to sleep and chronic malaise and fatigue, reduced capacity for work and poor school preformance. Patients are often plagued by a loss of smell or taste caused by nasal oedema and by postnasal drip with cough. Structural facial and dental problems can result from chronic allergic rhinitis. Constant upward rubbing of the nose (allergic salute) can cause a permanent transverse crease across the lower nose. Acute and chronic sinusitis are relatively common complications of allergic rhinitis. Nasal polyps are less common but bothersome. They require both specific therapy and generally improved management of the allergic state. The postnasal drip syndrome (PNDS) is one of the most common causes of chronic cough.

Treatment

Allergen avoidance is the mainstay of therapy for many patients but is not always practical. Regarding medication, nonsedating antihistamines and nasal steroids are relatively free of side effects, and are reasonably inexpensive.[17,18]

Table I: Effects of Medication Treatment.

Medication	Symptoms				
	Sneezing	Rhinorrhea	Nasal Congestion	Nasal Pruritus	Eye Symptoms
Antihistamine, oral	++	++	+	+++	++
Antihistamine, nasal	++	++	+	++	0
Antihistamine, ocular	0	0	0	0	+++
Nasal steroids	+++	+++	+++	++	++
Cromones, nasal	+	+	+	+	0
Cromones, ocular	0	0	0	0	++
Decongestants, oral	0	0	+	0	0
Decongestants, nasal †	0	0	++++	0	0
Anticholinergics, nasal	0	++	0	0	0
Antileukotrienes	0	+	++	0	++

0 = not effective for symptoms: + = mildly effective for symptoms: ++ = moderately effective for symptoms: +++ and ++++ = very effective for symptoms. † = Do not use > 3-5 d.

In children, the treatment should focus predominantly on prevention and be therapeutically as unagressive as possible. Allergen avoidance is an effective means of preventing symptoms triggered by indoor allergens such as house dust mite, animals or mould. Concomitant conjunctivitis frequently occurs in children with seasonal rhinitis, but is seldom reported in children with chronic allergic rhinitis.

The treatment should be matched to the symptoms. Prophylactic treatment to prevent the onset of significant symptoms is preferable to trying to control an ongoing problem, particularly in patients with moderate to severe disease. Oral antihistamines, nasal antihistamines and decongestants are initial treatment options for *mild intermittent rhinitis.* For *moderate to severe intermittent rhinitis,* additional options include a nasal steroid or cromone and immunotherapy may be considered. This also applies to *mild persistent rhinitis.* Patients with *moderate to severe persistent rhinitis* should be started on a nasal steroid and, on follow-up visit, an antihistamine may be added for itching and sneezing. It may also be necessary to add a decongestant on short-term oral steroid for congestion, but should the latter persist, a surgical referral should be considered. The effect of medication treatment is displayed in Table I.[19,20]

Oral antihistamines, particularly the newer non-sedating H1-receptor antagonists (e.g. levocetrizine, cetirizine, ebastine, fexofenadine, loratadine and deslora.tadine), are the primary agents in the treatment of allergic rhinitis in children. These newer agents are as effective as the older antihistamines in the treatment of allergic rhinitis symptoms except nasal blockage. They are less sedating and do not, in the elderly, cause urinary retention and problems of visual accommodation. Antihista. mines relieve sneezing, itching and discharge and have minimal effects on blockage. They are important first-line agents although less effective in one-third to one-half of patients. They provide only partial symptom relief for most patients, as histamine is only one of many mediators causing allergic rhinitis symptoms. *Topical antihistamines* (levocabastine, azelastine) have to be administered two to four times a day.

Cromones (i.e. sodium cromoglycate and nedocromil) reduce symptoms of sneezing, rhinorrhoea and nasal itching but tend to be less effective in the prevention of nasal congestion. Unfor tunately they have to be administered four times a day and the cromone must come into contact with the entire mucous membrane. Should ten percent of the nasal lining not be reached by the spray, symptoms could possibly be evoked in the entire mucous membrane.

Decongestants are used in combination with other agents, particularly the antihistamines, to relieve nasal blockage. Oral decongestants are alpha-adrenergic agonists that act by constricting blood vessels in the nasal mucosa, but can also cause side-effects, such as tremor, insomnia and nervousness. They may also aggravate certain other medical conditions, such as restricting urinary flow in males and they are contra-indicated in patients with hypertension of glaucoma. Topical decongestants such as phenylephrine and oxymetazoline relieve nasal congestion. However, the risk of secon.dary congestion allows only short-term use. It is dangerous to give topical vasoconstrictors to children under the age of one year due to the narrow range between therapeutic and toxic doses.

Intranasal corticosteroids are considered first-line in allergic rhinitis, because they relieve all the major nasal symptoms, including blockage. Since they primarily affect the late phase of the allergic reaction, they must be administered prophylactically on a regular basis. Maximum benefit appears during the second week of treatment, with onset of relief usually occurring after a week.

Intranasal absorption of the various steroids from the relatively small mucosal surface area is likely to be 30 to 40 percent of the deposited drug. Systemic effects may thus be seen in patients receiving concomitant treatment with corticosteroids for rhinitis and asthma. Although there is some reluctance to prescribe topical cortico.steroids to children with allergic rhinitis because of concerns about long-term systemic adverse effects, to date there have been virtually no adverse reports in the literature. Ocular symptoms in seasonal allergic rhinitis should be controlled with the topical application of cromoglycate or an antihistamine to the eye. The combination use of oral antihistamines and intranasal corticosteroids, which appears to offer only a marginal benefit compared with the use of intranasal steroids alone, should be reserved for patients with extensive hay fever symptoms over and above nasal symptoms. The cost of combination therapy should be carefully considered, par ticularly longer ter m therapy.

Immunotherapy usually results in only partial amelioration of symptoms. It is expensive, requires long-term treatment and compliance is poor. It should only be given to children who are at least six to seven years old. Strict guidelines for specific immunotherapy should be followed and suitable candidates carefully selected to maximise benefits.

Refer to a specialist

- Occupational rhinitis: symptoms occurring predominantly on work days.
- Nasal polyps: bilateral chronic nasal congestion with variable sneezing and discharge but with significant olfactory disturbance.
- Rhinitis medicamentosa: persistent rebound congestion as a result of intranasal decongestant abuse.
- Malignancy: continuous nasal congestion, particularly if unilateral, with bloodstained secretion or both.
- When specific immunotherapy is being considered.

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