

Allergic Rhinoconjunctivitis – An Overview

C. H. Katelaris

Institute of Immunology and Allergy Research, Westmead Hospital, Sydney, Australia

Key words: allergic rhinoconjunctivitis.

Acta Ophthalmol. Scand. 2000; 78: 66–68
Copyright © Acta Ophthalmol Scand 2000. ISSN 1395-3907

Allergic Rhinoconjunctivitis (AR/C) is a common and troublesome condition which afflicts over a third of our population. Neither the impact of this condition on quality of life nor its huge economic burden to the community has been fully appreciated in the past. This brief review contains a summary of the pathophysiology, clinical presentation, epidemiology and strategies for the management of this common condition.

Pathophysiology

Individuals with AR/C possess IgE antibodies bound to high affinity receptors on mast cells and basophils, as well as low affinity IgE receptors on a number of other cells including eosinophils, platelets and monocytes. Allergic inflammation is initiated following triggering of the mast cells by cross-linking of IgE antibodies by the relevant antigens. Chemical mediator release in this early phase is responsible for the classical symptoms of sneezing, itching, watery rhinorrhoea and nasal congestion. Histamine is one of the most important mediators of this early-phase response. Its release causes stimulation of sensory nerve fibres not only producing the symptoms already outlined, but also causing excitation of the parasympathetic reflexes which contribute to vasodilation and mucus secretion. In addition to a number of mediators, mast cell degranulation results in the release of chemotactic factors, chemokines and cytokines, all of which act to recruit inflammatory cells into the nasal mucosa.

The late-phase reaction occurs as a result of the upregulation and expression of leukocyte endothelial adhesion molecules

by the mast cell-derived cytokines and other mediators. The upregulation of specific adhesion molecules permits chronic inflammatory cells such as eosinophils to migrate into nasal, sinus and conjunctival tissues. Eosinophil accumulation contributes to the pathogenesis by the production of chronic inflammation. When repeated allergen exposure occurs, the chronic inflammation produced lowers the threshold for other reactions. This phenomenon, known as the priming effect, explains why lower levels of allergen are required for triggering of symptoms as the pollen season advances.

Classification

AR/C is traditionally classified as seasonal or perennial; the former triggered by pollens – trees, grasses or weeds – while allergens such as house dust mites and animal danders are responsible for year long symptoms. However, in many parts of the world, including the eastern seaboard of Australia, there are very long pollination periods with pollen allergy resulting in almost perennial symptoms. In some parts of the world, mould spores in the outdoor air may show seasonal variation while in other parts they are responsible for perennial symptoms.

Diagnosis

The main symptoms of AR/C are itching and irritation in the nose, bouts of sneezing, watery rhinorrhoea, nasal congestion, itchy eyes with tearing and swelling around the eyes. This symptom complex may be accompanied by itching of the throat, palate and ears. The symptom se-

verity may range from nuisance level to incapacitating.

A clinical diagnosis of allergic rhinitis can be made when the patient displays the characteristic signs and symptoms of rhinoconjunctivitis. It is important to remember that those with chronic perennial AR/C may only complain of nasal blockage or non-specific symptoms such as headache, fatigue or poor concentration and this may be particularly so in school age children with chronic AR/C.

A history of other atopic disorders such as atopic dermatitis or asthma and the presence of these disorders in other family members strengthens the case for the diagnosis.

Allergic conjunctivitis is seen very commonly in those presenting with a history consistent with allergic rhinitis although it may not be the presenting complaint. Up to 90% of individuals with classic pollen-induced symptoms will have some degree of allergic conjunctivitis while approximately 50% of house dust mite-sensitive individuals with perennial allergic rhinitis will have troublesome eye symptoms.

Confirmatory tests are important, firstly to confirm the allergic nature of the condition and secondly, to identify the allergen(s) responsible. The allergens provoking specific IgE responses may be identified by skin prick tests *in vivo* or by the performance of the various *in vitro* assays for specific IgE antibodies.

Epidemiology

Epidemiological studies have identified an increase in the prevalence of allergic rhinoconjunctivitis over the last 2 decades

and this increase is evident in studies from a number of countries. A progressive increase in hayfever has been demonstrated in surveys of general practice in Wales and England (1). In separate surveys, the annual period prevalence of hayfever consultations increased from 10.6/1,000 in 1970–71, to 19.8/1,000 in 1981–2. A similar doubling in the same decade is also evident in a Swedish study (2.) which surveyed Swedish conscripts. This study identified a prevalence of 4.4% in 1971 and 8.4% in 1981. By comparison, data from Australia suggests a much higher prevalence in this community. In a study of a population – based cohort of adults in Tasmania, Hopper et al. (3) have demonstrated the adult prevalence for hayfever has risen from 19.2% in 1968 to 41.3% in 1991–93.

The impact of AR/C

A number of papers have recently explored the impact of AR/C on the quality of life of those who suffer from the condition (4, 5). Patients with rhinitis are not just troubled by nasal symptoms but are limited in their ability to do everyday activities. Concentration is impaired and other associated symptoms such as headache are troublesome. Sleep may be impaired, social interaction may be limited and there is an impact on emotional well being.

When significant nasal obstruction is present over a long period, many complications may arise. In childhood, chronic obstruction may contribute to Eustachian tube dysfunction, otitis media, speech abnormalities, abnormalities in facial growth and dental development, while in adults, problems such as halitosis (as a consequence of mouth breathing), snoring, worsening of sleep apnoea and the development of sinusitis may result. Asthma co-exists in a significant number of patients with AR/C.

The economic impact of allergic rhinitis is considerable. At a personal level, loss of earnings may occur because of sick leave and reduced productivity. Personal income is spent on medications and allergen reduction strategies. For the community, the cost is also impressive. In the United States, AR/C gives rise to more than 20 million physician visits annually and costs the US economy billions of dollars each year. In Australia last year, almost half a million sick days were taken because of "allergies". Antihistamines are one of the most commonly prescribed medications—approximately 30

million dollars are spent annually on them; 16 million dollars are spent on nasal sprays and 4–5 million dollars on eye drops.

Management strategies

Treatment options consist of allergen avoidance, pharmacotherapy with an ever-increasing list of agents available, and allergen specific immunotherapy. The complexity and variety of available treatments has led a number of professional bodies to issue guidelines for the management of AR/C in adults and children (6, 7).

Successful management requires more than providing a script for medication. The treating doctor needs a clear understanding of the underlying mechanisms so treatment choice has a rational basis; the condition is generally one which is long lived, and treatment success will depend on patient compliance with the management strategies outlined by the physician.

Management must begin with a correct diagnosis followed by counselling about the condition. Although it is a "simple" problem, AR/C at present is incurable, and patients will need to manage their problem for decades. The first step is guidance in allergen reduction or avoidance where this is possible. As people spend more time indoors, environmental control measures are focused on limiting exposure to house dust mites, animal danders, moulds and cockroaches.

An array of pharmacological agents is now available which provides symptomatic relief; other agents have anti-inflammatory properties and are capable of bringing the condition under good control.

Antihistamines or H₁ receptor antagonists are drugs which act rapidly to antagonise the H₁ receptor and therefore may relieve the symptoms produced by histamine binding to its receptor – sneezing, watery rhinorrhoea and itching of the nose, eyes and palate. Many of the newer, non-sedating agents also possess certain "anti-allergic" properties which may have a more profound effect on allergic inflammation (8). As a class, they display avid binding to the H₁ receptor and have a quick onset of action. Most cause no more drowsiness than placebo, however, both acrivastine and cetirizine have been associated with slightly more daytime drowsiness than placebo at recommended doses (9). Two non-sedating agents – terfenadine and astemizole have

been associated with ventricular arrhythmias such as torsades de pointes (10). This rare complication resulted when greatly elevated drug levels occurred as a result of certain drug interactions or in the presence of significant liver disease. Both agents have now been withdrawn from the market. The major metabolite of terfenadine, fexofenadine is now marketed widely; extensive clinical studies have shown that it is not associated with this side effect.

When antihistamines are used on a regular basis, particularly in adults, they may be associated with drying of the conjunctiva, the symptoms of which are often mistaken as worsening of the accompanying allergic conjunctivitis. Such individuals should be encouraged to use lubricant eye preparations if antihistamines are to be taken regularly.

Although the older, "sedating" antihistamines are still available and remain popular because they are significantly cheaper than the newer agents, they have many ill effects including fatigue, sedation and performance impairment (11) and are therefore no longer the drugs of choice.

Anticholinergic therapy with the use of topical ipratropium bromide has a place in controlling the watery rhinorrhoea which is so troublesome to many sufferers. However, it has no effect on all the other manifestations. It is particularly good for those individuals who experience rhinorrhoea with exposure to cold air and spicy food.

Topical nasal decongestant sprays relieve nasal congestion rapidly, are available over the counter and are thus popular with sufferers. They work by constricting the smaller arterioles, thus reducing blood flow and relieving mucosal oedema. Unfortunately, overuse of decongestants may cause rebound nasal congestion and rhinitis medicamentosa. Their use should be confined to short-term application for patients with marked nasal blockage to allow application of more appropriate agents such as topical corticosteroid sprays.

Oral decongestant agents work in a similar fashion, however, they have a systemic effect increasing the risk of complications. They should be avoided in individuals with cardiovascular disease, glaucoma, diabetes and thyrotoxicosis. Combined antihistamine/decongestant preparations may provide greater symptomatic relief than either agent alone.

Anti-inflammatory agents include cromolyn sodium and intranasal steroids.

Cromolyn sodium has proven to be effective for the treatment of AR/C, but it is best used prophylactically. Its need for frequent administration, four to six times per day is an impediment to compliance in many patients. It is particularly used in children and in the elderly.

Intranasal steroid sprays relieve all the symptoms of AR/C and comparative studies have shown them to be superior (12) to both antihistamines and cromolyn sodium. In addition, a meta-analysis of their use in AR/C demonstrated that they relieve the accompanying eye symptoms more effectively than antihistamines (12). Intranasal steroids inhibit both the early and late phase responses to allergen challenge and influence a number of cells involved in nasal allergic inflammation including reduction in the number of eosinophils in the nasal mucosa and a reduction of mast cells and T cells, explaining their superior efficacy.

Side effects are usually minor and local e.g. slight bleeding and irritation. While the risk of systemic side effects is very small, it is prudent to use the lowest effective dose, particularly in children and in those already using inhaled steroids for asthma. Onset of action is slower than that of antihistamines and decongestants so patients must be warned of this in order to enhance compliance.

Allergen specific immunotherapy (SIT) modifies the immune response and results in a reduction in allergic inflammation. It is used in conjunction with medication, but it eventually reduces the need for

pharmacotherapy. Its efficacy is well established (13) but results are best when the patient has a single allergic sensitivity. SIT should only be undertaken by appropriately trained physicians whose premises are equipped with necessary resuscitation facilities as rare adverse events such as anaphylaxis may occur. Newer approaches to immunotherapy include alternative routes of administration such as nasal, oral and application to the oral mucosa.

In practice, patients with AR/C will use a combination of modalities in order to manage their troublesome symptoms.

A condition as common as AR/C must be successfully managed in general practice. Specialist referral should be considered for those who have developed complications or who have not responded well to the medication approaches listed above.

References

1. Fleming DM, Crombie LD. Prevalence of Hayfever in England and Wales. *Br Med J* 1987; 294: 279–283.
2. Aberg N. Asthma and allergic rhinitis in Swedish conscripts. *Clin Exp Allergy* 1989; 19: 59–63.
3. Hopper JL et al. Increase in self-reported prevalence of asthma and hayfever in adults over the last generation: a matched parent – offspring study. *Aust J public Health* 1995; 19: 120–124.
4. Juniper EF, Guyatt GH. Development and testing of a new measure of health status for clinical trials in rhinoconjunctivitis. *Clin Exp Allergy* 1991; 21: 77–83.
5. Bousquet J, Bullinger M, Fayol C, et al. Assessment of quality of life in patients with perennial allergic rhinitis with the French version of the SF-36 health Status Questionnaire. *J Allergy Clin Immunol* 1994; 94: 182–188.
6. International rhinitis management working group. International consensus report on the diagnosis and management of rhinitis. *Allergy* 1994; 49 Suppl 19.
7. Diagnosis and management of rhinitis: complete guidelines of the joint taskforce on practice parameters in allergy, asthma and immunology. American Academy of Allergy, Asthma and Immunology. *Ann Allergy Asthma Immunol* 1998; 52: 478–518.
8. Bousquet J, Lebel B, Chanal I, Morel A, Michel F-B. Antiallergic activity of H1 receptor antagonists assessed by nasal challenge. *J Allergy Clin Immunol* 1988; 82: 881–887.
9. Falliers CJ, Brandon ML, Buchman E et al. Double-blind comparison of cetirizine and placebo in the treatment of allergic rhinitis. *Ann Allergy* 1991; 66: 257–262.
10. Nightingale SL. Warning issued on non-sedating antihistamines terfenadine and astemizole. *JAMA* 1992; 266: 705.
11. Simons FER. H1 receptor antagonists. Comparative tolerability and safety. *Drug Safety* 1994; 10: 350–380.
12. 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.
13. European Academy of Allergology and Clinical Immunology. Immunotherapy. In: Malling H-J, Weeke B, editors. EAACI Position Papers. *Allergy* 1993; 48 Suppl 14: 7–35.