Recommended management and recent advances in allergic rhinitis

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Allergic rhinitis is a common and under-treated condition and is often a precursor to asthma in children. Our Drug review discusses diagnosis, recommended management and recent advances in treatment, followed by sources of further information and an analysis of the prescription data.

The prevalence of allergic disorders such as allergic rhinitis, allergic conjunctivitis and bronchial asthma has steadily increased in nearly all Western industrialised countries during the past three decades. It is estimated that allergic rhinitis affects over 20 per cent of the UK population and up to 40 per cent of children. Most patients with allergic rhinitis can be easily and effectively managed in the community but both patients and GPs describe low levels of satisfaction when treating allergic rhinitis. Studies suggest that patients are undertreated, with only 32 per cent of patients reporting good symptom control in UK primary care. Affected patients sometimes turn to complementary treatment because of a poor clinical response to treatment and fear that prolonged use of conventional medications may be related to potential adverse effects.

This article will summarise key points in the treatment and management of allergic rhinitis, including recent advances and explains how this can become a highly effective and satisfying condition to treat.

Impact of allergic rhinitis

Traditionally, allergic rhinitis has been classified as seasonal or perennial. This works well in countries with well-defined seasons such as the UK. In 2001, the Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines reclassified allergic rhinitis into intermittent and persistent categories, with subdivision into mild or moderate-severe disease. In 2008, the British Society for Allergy and Clinical Immunology (BSACI) published detailed guidelines describing the management of rhinitis, and UK experts were of the opinion that the classification of allergic rhinitis into seasonal or perennial remains useful in UK clinical practice, and can be used alongside ARIA guidelines.

Allergic rhinitis is no longer considered a ‘benign’ disease – patients with allergic rhinitis, whether seasonal or perennial, are at higher risk of developing asthma compared
Allergic rhinitis also predisposes patients to chronic otitis media, chronic rhinosinusitis and obstructive sleep apnoea, and leads to academic underachievement. Teenagers with seasonal allergic rhinitis are significantly more likely to drop a GCSE grade, compared to their nonallergic peers.

Diagnosis
The four major clinical features of allergic rhinitis are:
• itching (nose, palate, oropharynx and ears)
• sneezing (which may be paroxysmal)
• rhinorrhoea (can be anterior or lead to postnasal drip)
• nasal congestion (although this is not the dominant symptom).

Allergic rhinitis is caused by a number of inhalant allergens including: mixed tree, birch and grass pollens, cat, dog, house dust mite (HDM) and moulds. Allergy to HDM is the most common indoor allergen causing perennial allergic rhinitis. However, objective evidence of raised specific IgE to an inhalant allergen is essential before a patient spends time and money undertaking extensive allergen avoidance measures.

In UK general practice, diagnosis by history alone resulted in false-positive identification of allergen triggers of 32 per cent for cat allergy, 48 per cent for grass pollen, 75 per cent for HDM, 54 per cent for tree pollen and 27 per cent for dog when compared with formal allergy assessment including allergy skin testing. There is no value in extensive HDM avoidance or removal of a family pet if the sufferer is nonatopic and has no relevant allergic sensitivities. Thus objective assessment of IgE sensitivity improves accuracy in identifying allergenic triggers and accurate diagnosis.

Furthermore, once specific IgE to an inhalant allergen is detected, the test must be interpreted correctly and the clinician must distinguish between sensitisation and allergy. At least 15 per cent of people with a positive skin test do not develop symptoms on exposure to the relevant allergen, so the clinical history must be consistent with skin tests to confirm a clinically relevant sensitivity. For example, if a patient has year-round symptoms, severe rhinosinusitis and nasal polyps, an isolated positive skin test to birch pollen is almost certainly irrelevant. However, they have a high negative predictive value and therefore the patient with negative skin prick tests or no evidence of raised specific IgE is likely to be genuinely nonallergic.

Role of oral antihistamines
Oral antihistamines are widely used as a first-line treatment in mild-to-moderate intermittent and mild persistent allergic rhinitis. They are popular with patients due to their rapid onset of action and easy availability and are most effective in reducing symptoms of itch, sneeze and rhinorrhoea. In patients with perennial symptoms regular usage is more effective than dosing ‘as and when’.

While first-generation antihistamines (eg chlorpheniramine or diphenhydramine) remain effective, they cause drowsiness and reduce academic performance and therefore should be avoided where possible. At the recommended doses, all second-generation antihistamines are less sedating compared to their predecessors and have fewer major drug interactions and therefore should be prescribed instead. Additionally, the second-generation antihistamines desloratadine, fexofenadine, cetirizine and levocetirizine have modest effects on nasal blockage.

Role of corticosteroids
Intranasal corticosteroids (ICS) are presently the most effective overall treatment for allergic rhinitis and are first-line therapy for adults in moderate-to-severe cases of allergic rhinitis or in individuals who are still symptomatic despite the regular use of antihistamines. ICS relieve all symptoms of allergic rhinitis, including nasal blockage, and meta-analysis shows that are more effective than antihistamines. They act by suppressing inflammation in the nasal mucosa leading to a reduction or resolution of symptoms. There is some worry over the long-term effects of using steroids but fluticasone...
furoate (Avamys), fluticasone propionate (Flixonase) and mometasone (Nasonex) have little systemic absorption. No significant difference in the number of symptom-free days or quality of life has been reported between the three drugs.8 Both fluticasone furoate and mometasone have been shown to reduce symptoms of allergic conjunctivitis as well as allergic rhinitis.9,10

Systemic corticosteroids are rarely indicated in the management of rhinitis. However, there are occasions when a short three-to-five-day course of oral steroids may be beneficial. In particular, ICS sprays will not be effective of course if the nostril is completely blocked and the drug can not enter the nasal cavity and therefore oral steroids may be co-prescribed along with a topical nasal corticosteroid if a patient is congested.2

Depot corticosteroid injections, eg triamcinolone (Kenalog), have been used in the past for the treatment of allergic rhinitis. While often effective, it is now considered that they have no place in the management of allergic rhinitis because of their associated risks and side-effects – particularly osteoporosis.2

**Difficult-to-treat allergic rhinitis**

When a patient is still symptomatic despite treatment with oral antihistamines and ICS, the first stage is to check adherence and correct technique.2 Clinical practice suggests that most patients who have found ICS unhelpful have not persisted with treatment for an adequate period.11 Patients should be advised that the onset of action of ICS is slow and that they should be used regularly for a minimum of two weeks before considering them unsuccessful.12 Patients with seasonal allergic rhinitis should commence therapy two weeks before the pollen season as this improves efficacy.2,13

When using ICS patients should be given clear instructions in order to maximise their response to treatment. Individuals should be advised to: direct the nasal spray laterally (rather than medially towards the nasal septum), to site the two puffs in different places and not to sniff for at least 10 minutes after spraying (see Figure 1). All these measures will increase benefit. Tipping the head back and sniffing hard decreases treatment efficacy (the spray will run down the nasopharynx) and patients should be advised not to do this.

To maximise effect all patients should be advised to douche with saline prior to using their nasal spray. Saline douching clears mucus from the nasal cavity permitting local absorption of the ICS, thereby increasing its effectiveness. A number of over-the-counter saline preparations are available in the UK. The use of saline douching has demonstrable benefit in symptom reduction in children and adults with seasonal rhinitis as well as in chronic rhinosinusitis.14,15

The next stage is to consider additional treatments.

**Combined ICS and antihistamine**

Dymista (a novel formulation of azelastine and fluticasone propionate) in patients with moderate-to-severe seasonal allergic rhinitis, was shown in a multicentre randomised double-blind placebo controlled-trial (n=3982) to significantly reduce the symptoms score compared to fluticasone propionate and intranasal azelastine (Rhinolast) alone. The effect was better and faster than with the individual drugs alone and remarkably one in eight patients reported complete symptom resolution, which is surprising considering that the majority of patients had severe seasonal allergic rhinitis.16

The trial did not evaluate the effect of Dymista in patients with perennial allergic rhinitis nor compare the effect of a Dymista with concomitant use of an oral antihistamine and a nasal corticosteroid, but as azelastine has superior effects to oral antihistamines17 and a combined nasal corticosteroid/antihistamine preparation is likely to encourage adherence it is the author’s opinion that Dymista should be trialled in patients with difficult to treat allergic rhinitis before consideration of allergen immunotherapy.

**Leukotriene receptor antagonists**

Leukotriene receptor antagonists (LTRAs) block the effects of cysteinyl leukotrienes, which are important proinflammatory mediators of nasal allergic reactions and whose release locally induces nasal obstruction. Although some efficacy with LTRAs has been shown in allergic rhinitis, the spectrum of individual responsiveness remains variable and the combination of an antihistamine and an LTRA is no more effective than an ICS alone. However, it is worthwhile considering the prescription of an LTRA in patients with difficult allergic and concurrent asthma, in addition to treatment with antihistamines and topical nasal steroids.2

**Referral for allergen immunotherapy**

Allergen immunotherapy should be considered in patients who, despite optimisation of pharmacotherapy, remain acutely symptomatic.18 Patients should be referred to a specialist allergy centre for consideration of immunotherapy. The BSACI website provides a list of suitable allergy clinics (www.bsaci.org). Indications for immunotherapy are listed in Table 1.

Allergen immunotherapy involves the regular administration of specific semipurified allergen extracts. It is a highly suitable and effective treatment for patients with moderate/severe allergic rhinitis that persists despite conventional treatments. It should only be given in secondary care under

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### Table 1. Indications for immunotherapy

- patients with seasonal allergic rhinitis, where symptoms have not adequately responded to conventional pharmacotherapy
- patients with IgE-mediated allergic rhinitis where pharmacotherapy induces undesirable side-effects
- selected patients with animal dander or house dust mite allergy in whom rigorous allergen avoidance and reasonable pharmacotherapy fails to control symptoms
- systemic reactions caused by bee or wasp venom allergy (outside the scope of this article)
clinical supervision due to the risk of a systemic allergic reaction.

The allergen extracts can be administered either subcutaneously or sublingually with a view to desensitising the patient’s allergic reaction when the sensitising allergen is subsequently encountered under ‘natural exposure’ conditions. In asthma the risk-benefit ratio is less favourable than for rhinitis and it is not routinely recommended in the UK.18

**Sublingual immunotherapy**

Despite the many benefits of subcutaneous immunotherapy (SCIT), the potential for anaphylaxis exists with each injection and patients need to take time off work to attend hospital appointments.

Sublingual allergen administration is an approved treatment for allergic rhinitis and involves placement of an allergen extract under the tongue for one to two minutes until it dissolves. Sublingual immunotherapy (SLIT) has great therapeutic potential for allergic rhinitis and allergic asthma. It is convenient and safer than subcutaneous immunotherapy, but its effectiveness and duration of effect require study.18 In seasonal allergic rhinitis SLIT to grass pollen has been shown to reduce symptom and medication scores and decrease asthma symptoms.20

One study evaluated 63 randomised controlled trials involving 5131 patients from 4 to 74 years of age.21 They found strong evidence that SLIT improved asthma symptoms and
moderate evidence for its decreasing rhinitis or rhinoconjunctivitis compared with the comparator and found reduced requirements for other medications. No life-threatening adverse events were observed.

However, the first meta-analyses comparing SCIT to SLIT suggest that SCIT is more effective than SLIT in controlling symptoms and in reducing the use of antiallergic medications in seasonal allergic rhinoconjunctivitis to grass pollen. Thus, as yet the size and duration of the benefit of SLIT compared to SCIT is not clear, and therefore further studies are required optimising allergen dose and patient selection.

Looking to the future
The risk of developing asthma is approximately six times higher in patients with HDM allergy compared to those allergic to pollens. This may reflect the ubiquitous nature of the allergen. Furthermore, allergic rhinitis often precedes asthma and is a relevant independent risk factor for its development.

In 2013 the first large-scale randomised double-blind placebo-controlled study evaluated the efficacy of HDM sublingual tablets in relieving HDM-associated allergic rhinitis symptoms. The authors found that 12 months of sublingual HDM tablets was efficacious and well-tolerated, with onset of action after four months. Efficacy was maintained in the treatment-free follow-up year. The intriguing question is whether administering SLIT to HDM in children with allergic rhinitis may have a disease-modifying affect and reduce the chance of an individual developing asthma in the future.

Conclusion
Allergic rhinitis is increasing in prevalence and it is no longer viewed as a ‘benign condition’. In children, it is often a precursor to asthma and teenagers with allergic rhinitis are significantly more likely to academically underachieve. For mild allergic rhinitis second-generation antihistamines are the first-line treatment and for moderate/severe allergic rhinitis ICS are the treatment of choice. Patient education is critical as treatment failure is most often due to reduced adherence and poor technique in applying topical nasal sprays or drops.

For patients with disease that fails to respond to oral antihistamines and ICS, combined ICS/antihistamine sprays and LTRAs should be considered. If there is a poor response to pharmacotherapy referral to an allergy clinic for consideration of allergen immunotherapy is appropriate.

Recommended management of allergic rhinitis is outlined in Figure 2.

References

Declaration of interests
None to declare.

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Resources
Guidelines


Prescriber articles

### Prescription review

In 2013, GPs in England wrote 12.9 million prescriptions for oral antihistamines at a cost of £33 million, and 6.8 million prescriptions for nasal preparations costing £46 million. Many of these products are also available without prescription.

Non-sedating agents are now the most frequently prescribed oral antihistamines and among the least expensive, with cetirizine and loratadine both cheaper than chlorpheniramine and together accounting for 60 per cent of volume and 33 per cent of spending. Newer non-sedating agents – desloratadine, levocetirizine and fexofenadine – are much less widely used (15 per cent of volume) and more expensive (39 per cent of costs) though fexofenadine, which ranks top for spending, is third in prescribing frequency.

Beclometasone dipropionate, fluticasone propionate and mometasone together account for 83 per cent of nasal preparations and for 81 per cent of spending. Beclometasone dipropionate is by far the cheapest of the three but the cost of fluticasone propionate is inflated by the preparation for nasal polyps (Flixonase Nasule). The number of doses varies between brands and preparations from 60 to 200 and this should be taken into account when comparing costs.

**Table 2.** Number of prescriptions and costs for drugs used to treat allergic rhinitis, England, 2013

<table>
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<tr>
<th>Drug</th>
<th>No. scrips (000s)</th>
<th>NIC (£000s)</th>
<th>NIC per scrip (£)</th>
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