CLINICAL GUIDELINE

Clinical Management of Allergic Rhinitis – the Allergy Society of South Africa Consensus Update

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Inadequately controlled allergic rhinitis in asthmatic patients can contribute towards increased exacerbation of asthma, poorer medical control and an increased demand on medical resources. If properly diagnosed and treated, a significant improvement in the patient's wellbeing and quality of life (QOL) is to be expected, with the added bonus of the pharmaco-economic benefits that result when allergies are cured.

Since the first comprehensive South African Consensus statement,[1] there have been several publications on new forms of therapy for patients with allergic rhinitis.[2-4] The Allergy Society highlights advances and recommends the following.

1. Classification of allergic rhinitis

The International Allergic Rhinitis and its Impact on Asthma (ARIA) Workshop report, supported by the World Health Organization (WHO) and compiled by experts from 16 countries, was published in the *Journal of Allergy and Clinical Immunology*.[2] The ARIA document reclassified allergic rhinitis into 'persistent' or 'intermittent', which may in turn be 'mild' or 'moderate-severe'. This new classification has been accepted by the World Allergy Organization and the European Academy of Allergy and Clinical Immunology (EAACI) and is now applied globally, replacing the old classification of 'perennial' or 'seasonal' rhinitis. The ARIA classification of allergic rhinitis also brought it in line with the Global Initiative for Asthma (GINA) classification of asthma, since rhinitis and asthma are considered components of the united airways, which share the same aetiology and pathology. 'Intermittent' refers to rhinitis with symptoms lasting less than 4 weeks or for less than 4 days per week. 'Persistent' refers to rhinitis lasting more than 4 days a week for more than 4 weeks per year. Mild rhinitis does not interfere with sleep, sport, leisure or daily activities. Moderate to severe rhinitis affects sleep, work, daily activities, sport, leisure, school or causes troublesome symptoms.[3,4]

Different pharmacological treatments for mild, moderate or severe, intermittent or persistent rhinitis have been assessed using evidence-based medicine criteria[3,4] and applied to South Africa.[5]

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In view of the long pollen seasons in Gauteng and Limpopo provinces, the Eastern Cape, the Eastern Free State and the Western Cape, most patients who have pollen-induced rhinitis have persistent rhinitis.

2. Assessment of rhinitis patients should be more comprehensive, and include non-nasal symptoms and quality of life

Patients with allergic rhinitis typically feel 'under par' and are troubled by their disease. The QOL of rhinitis subjects has been reported to be worse than that of asthmatics.[6] Doctors should assess their rhinitis patients holistically rather than just focusing on the nose.

The Juniper Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ)[6] is a validated method of assessing QOL in patients with rhinitis and includes the following domains: activities, eye symptoms, nasal problems, practical problems, emotional problems, non-hayfever symptoms and sleep. These are scored using a 0 - 6 severity scoring system and provide a comprehensive assessment of allergic rhinitis patients. Combined with an assessment of their medication requirements, QOL scores can be used to calculate a Global Severity Score (GSS),[7] which may also be used to monitor improvement and response to treatment.

3. Investigation of allergy in rhinitis patients in South Africa seldom requires large investigative panels

Skin-prick testing remains the least expensive method of testing and will effectively diagnose the relevant allergies in over 80% of allergic rhinitis patients. A testing panel should include house dust mites (Der-p-1, Der-f-1), Bermuda grass, rye grass, and cat, dog, cockroach and fungal spores (*Cladosporium*, *Alternaria* and *Aspergillus*) in all South African regions, but should the history suggest it, plane and oak trees, maize pollen (*Zea mays*), and cypress and eucalyptus could be added.

Pollen allergies in the Savannah, the Northern Province, Mpumalanga and Limpopo Province are invariably because of sensitivity to Bermuda, rye and eragrostis grass pollens.

Some patients with rhinitis are affected by foods. Non-immunoglobulin E (IgE)-mediated food-induced rhinitis appears to be more common than previously thought. These food intolerance reactions are usually accompanied by negative specific IgE tests to the relevant allergens. Some adverse reactions are due to preservatives such as sulphites (e.g. in wine, beer and soft drinks) that cause nasal stuffiness and other symptoms.

The CAP RAST is a sensitive and specific blood test, and a screening panel should include at least house dust mites (Der-p-1 and Der-f-1), a grass mix (including Bermuda grass) and a mould mix (Cladosporium, Aspergillus and Alternaria). Based on history and exposure a further 400 allergens can be tested for using CAP RAST (e.g. cat, latex, foods, etc.), but these should not form part of routine screening tests unless suggested by the history.

The Phadiatop test may be used as a screening blood test if no useful history is available to assist in the selection of a specific test, or when an inhalant allergy specifically needs to be excluded (e.g. in suspected vasomotor rhinitis, or when dermatographism is present).

Vasomotor components (e.g. sensitivity to perfumes, temperature changes, air-conditioning and diesel fumes) may occur in non-allergic rhinitis but may also be present in some patients with true allergic rhinitis.

4. Antihistamines

In addition to long-acting second-generation antihistamines such as cetirizine, loratadine and fexofenadine, which are effective and safe, new-generation antihistamines, desloratadine and levocetirizine, are available in South Africa. They lack sedation, cardiotoxic effects (QT prolongation) and interaction with CYP450 enzymes, and nonspecific antimuscarinic effects. The old 'first-generation' antihistamines are not recommended for the treatment of allergic rhinitis (e.g. chlorpheniramine, diphenhydramine, hydroxyzine, etc.). The sedating effects of antihistamines are less pronounced in children than adults. First-generation antihistamines are effective for symptom relief and are the only antihistamines currently available in some public-sector institutions.

The sedating effects of first-generation antihistamines may be equivalent to those experienced with alcohol consumption[8] and may lead to motor vehicle accidents, poor school performance[9] and ICU admission for toxicity. They should only be used with due caution when second-generation antihistamines are unobtainable, and are better used at night and on an 'as-required' basis. Patients must be informed about possible sedating effects of these antihistamines when they are prescribed.

First-generation antihistamines are present in many formulations for the treatment of influenza, cough and pain and may cause unexpected and at times severe sedation.[5] New-generation antihistamines have also been shown to have anti-inflammatory effects, which may be of clinical significance in alleviation of the nasal eosinophilia so characteristic of allergic rhinitis.

5. Intranasal steroids

Intranasal steroids remain the most potent all-round anti-inflammatory medications for the management of allergic rhinitis patients. However, proper instruction in their use is essential. The nozzle of the spray should be directed in an upward and lateral direction towards the inferior turbinates and not towards the nasal septum. Doses should be kept below a total of 400 µg beclomethasone equivalent per patient per day to avoid adrenal suppression, particularly in children, and special care is required in the case of patients who are also taking inhaled steroids for the treatment of asthma. Certain steroid drops (e.g. betamethasone) are potent, not usually recommended intranasally and should never be used for more than 10 days. Inhaled steroids are safe for long-term use and need not be discontinued when patients have an upper respiratory tract infection or sinusitis. In patients who also require inhaled steroids, doses should be minimised to avoid systemic side-effects from higher doses of steroids absorbed from the nose and respiratory tract.

6. Injected/oral steroids

Patients who have severe incapacitating disease should be assessed carefully before prescribing steroids via any route other than the intranasal route. Severe symptoms may result from complications such as infected sinusitis, polyps or undiagnosed allergies, and underlying reasons for more severe symptoms must be explored, preferably by a specialist.

Injected or oral steroids should only be used for severe incapacitating allergic rhinitis in adults for short periods (10 days). Long-term adverse effects of repeated courses of intramuscular treatment in the management of allergic rhinitis remain a concern. Some patients, when given injections of cortisone, appear cushingoid within 3 months (N Mygind, Denmark – personal communication).

A recent study in South Africa[10] showed that short-term adrenal suppression occurred within 2 weeks of 1 mg betamethasone given daily, which was easily reversible on discontinuing therapy. Long-term use of steroids by any route other than the intranasal route is not recommended. Oral and injected steroids should not be used for the treatment of paediatric allergic rhinitis.

In exceptional cases short-term oral steroids may be used where patients are unresponsive to a combination of antihistamines and intranasal steroids. Celestamine contains a first-generation antihistamine and may therefore be sedating. Intraturbinate steroid injections are not recommended.

Oral steroids in combination with sedating antihistamines are still widely used and often abused in the treatment of allergic rhinitis. No more than 4 such courses should be used per year, since such patients may well have other underlying nasal pathology (e.g. polyps, tumours, adenoids), which require the assessment of an ENT surgeon.

Patients must be informed that there are steroids in these medications and parents should be advised not to 'self-medicate' their children with unused medications.

7. Leukotriene receptor antagonists

With the launch of montelukast for patients in South Africa as young as 2 years of age, and its published beneficial effects in allergic rhinitis,[11,12] its role in the general management of rhinitis is being explored. It has been demonstrated that asthmatics who also had concomitant allergic rhinitis responded better to montelukast than those who did not suffer from allergic rhinitis.[12] Therefore montelukast may have a special niche as add-on therapy in asthmatics who also have allergic rhinitis, since its therapeutic effect has been shown to be equivalent to that of loratadine.[11] However, leukotriene receptor antagonists are less effective than intranasal corticosteroids. The combination of a leukotriene receptor antagonist and an antihistamine is significantly more effective than when either is used alone.[13]

Beneficial effects of leukotriene receptor antagonists also result from their anti-inflammatory effects on vascular permeability, eosinophils, and mucus production. In young children with allergic rhinitis and mild asthma it may therefore be effective as monotherapy. Since its clinical effects are rapid in onset (within 48 hours), a trial of 14 days is indicated and should be reviewed before chronic management is recommended for this indication. In patients who have asthma with aspirin sensitivity and nasal polyps (e.g. Samter's triad), montelukast is the drug of choice.

8. Allergen immunotherapy

Specific allergen immunotherapy (SIT) is the only form of therapy that can change the natural history of allergic rhinitis, prevent progression of disease and cure patients if they are selected carefully. Two forms of SIT are available, viz. SCIT (subcutaneous immunotherapy) and SLIT (sublingual immunotherapy).

Both the sublingual and injected (subcutaneous) routes are highly effective for patients with house dust mite allergies or grass pollen allergies.[14] In the sublingual route patients are given increasing concentrations of allergen, held under the tongue for 2 minutes before swallowing, for an initial build-up phase of 1 month followed by a maintenance course for 2 - 3 years.

The sublingual route (SLIT) is safer and is conveniently taken at home. It is therefore a suitable 'safe' form of immunotherapy in areas where specialised services required for injection allergy immunotherapy (SCIT), i.e. allergy immunotherapy clinics, are not available.

Only doctors who have undergone adequate basic training in this procedure should conduct SCIT. Recently, equivalent efficacy was reported for SCIT and SLIT, but SLIT was found to be safer.[15]

A recent Cochrane Review[16] showed that SLIT was effective and safe for both house dust mite and grass pollen-monosensitive rhinitis subjects.

Post-marketing studies have shown SLIT to be safe.[17,18] No serious adverse side-effects were reported in a review of the combined experience of the South African Allergic Rhinitis Working Group (SAARWG), representing over 200 patients in South Africa treated with SLIT for up to 3 years, on a named patient basis. Medication costs for patients receiving SLIT ha reduced by 75% in South Africa.[7]

Before undergoing immunotherapy, patients need to have skin-prick tests or blood RAST tests to confirm their specific allergy and to exclude polysensitisation.

Since immunotherapy vaccines are still unregistered with the Medicines Control Council (MCC), they must currently be approved by the MCC on a named patient basis before ordering and administration. Until SLIT is registered fully with the MCC the prescribing doctor is responsible for making the application and providing 6-monthly progress reports on such patients. Following approval from the MCC, vaccines currently obtained from Alk-Abello (Spain), Stallergenes (France) and Leti (Spain) may be used in patients who have the correct clinical indications.

Patients must be carefully instructed regarding the indications, administration and possible side-effects of immunotherapy before selecting either SLIT or SCIT. Treatment must be for a minimum of 3 years, and 6-monthly follow-up visits are recommended to assess symptom scores, ongoing medication requirements and QOL issues.

SLIT and SCIT dramatically reduce the requirements for ongoing therapy with intranasal steroids and antihistamines and are therefore cost-effective for selected patients.

Contraindications for SLIT or SCIT include polysensitisation to several unrelated allergen groups, older patients (over the age of 60 years), patients with thyrotoxicosis, coronary vascular disease, mental disorders, autoimmune diseases and hypertension.

9. Generic substitution

Although generic substitution of antihistamines and intranasal steroids for the treatment of allergic rhinitis is recommended by the Health and Pharmacy Act,[19] some patients do not do well, or improve clinically, on certain generic antihistamines and intranasal steroids. Some health funders and state

hospitals recommending certain branded generics without confirmation of clinical equivalence with the parent drug have exacerbated this. Trials showing clinical equivalence should be made available before a health provider recommends a generic alternative for the purposes of reimbursement. Where such information is not available the parent drug should be dispensed wherever possible.

10. Alternative rhinitis treatments

The place of complementary and alternative medicine in the treatment of allergic rhinitis has been reviewed.[20] There is no convincing scientific proof of efficacy for most complementary and alternative medicine treatments for rhinitis and asthma.

Patients should be warned that some alternative or herbal products may have side-effects, are expensive, and have not been shown to be superior in efficacy to evidence-based medicines.

11. Education of pharmacists and the public

In more than 60% of cases the first line of help for the allergic patient is the local pharmacy. Pharmacists must be educated on the diagnosis of 'allergic' versus 'infective' conditions of the nose, to avoid 'cold mixtures' and/or antibiotics being repeatedly prescribed for patients with allergies. Over-the-counter (OTC) intranasal vasoconstrictor drops are dangerous if used chronically and lead to resistant rhinitis or rhinitis medicamentosa.

Recent ARIA workshop guidelines for the management of allergic symptoms in the pharmacy have been published in the form of a pocket handbook; these guidelines are endorsed by the EAACI and the Royal Pharmaceutical Society of Great Britain.[21]

Wherever possible pharmacists should not recommend sedating antihistamines for rhinitis treatment.

The general public should be made aware of how to distinguish broadly between symptoms of a cold (e.g. sore throat, low-grade fever with rhinorrhoea, headache and malaise) from the typical symptoms of allergy (no sore throat, no fever, itchy throat, itchy eyes, itchy nose with runny or blocked nose, which is persistent for more than 10 days and has a seasonal or diurnal variation). Such symptoms necessitate specific allergy testing and specific allergy treatment by general practitioners or specialised allergy clinics.

Non-responsive allergic conditions should be referred to a specialist so as to diagnose and treat other conditions that may mimic or aggravate allergic rhinitis.

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