Diagnosis and Management of Allergic Rhinitis in Children

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Abstract

Allergic rhinitis is one of the most common chronic diseases in children. It is a Th2 type allergic disease. Diagnosis is based on the presence of typical symptoms and evidence of allergic sensitization. Up to one in three children with allergic rhinitis develop asthma, and up to 80% of children with asthma have allergic rhinitis.

The most common allergic triggers are house dust mites, grass, weed and tree pollens, cat and dog allergens, and indoor and outdoor mould.

Local allergic rhinitis is a distinct phenotype characterised by typical symptoms and history of allergic rhinitis with undetectable specific IgE, but a positive nasal provocation test to one or more allergens.

Treatment of allergic rhinitis consists of a three-step approach: allergen avoidance, pharmacological treatment with antihistamines or intranasal corticosteroids, and allergen immunotherapy.

Introduction

This article is the written report of an oral presentation at the VVK (Vlaamse Vereniging voor Kindergeneeskunde) conference on April 21, 2023 and is based on several guidelines and clinical practice (1-5). It provides an overview of the diagnosis and management of allergic rhinitis in children.

Allergic rhinitis (AR) is one of the most common chronic conditions in children. It is rarely seen in infants, but from the age of 2 years there is a gradual increase in the prevalence by 3-4% a year, with up to 15 % of 13–14 year olds being affected (6, 7).

Although it can have a significant impact on quality of life, it is often under-diagnosed and under-treated.

AR is a Th2 type allergic disease. In a sensitised individual specific IgE to an environmental allergen binds to mast cells and basophils in the nasal mucosa and causes a biphasic reaction. In the early phase, degranulation of inflammatory mediators (histamine, leukotrienes, prostaglandins, platelet activating factor (PAF)…) causes symptoms such as sneezing and rhinorrhoea, within minutes of exposure. In a late phase (hours after exposure) activated eosinophils migrate to the nasal mucosa and release additional mediators that trigger prolonged inflammation and nasal congestion.

Diagnosis and classification of AR

The diagnosis of AR is based on the occurrence of the typical symptoms and the presence of relevant allergic sensitisation, demonstrated either by skin prick test or specific IgE.

Typical symptoms for allergic rhinitis are: sneezing, itchy and /or runny nose, nasal obstruction and red itchy eyes. Headache, sore or itchy throat, cough and hearing loss can also be experienced. Symptoms can be very bothersome, preventing children from participating in their normal activities. AR can affect sleep, concentration and have an impact on school performance.

Clinical signs of AR include allergic shiners (dark circles under the eyes), Denys Morgan folds (creases under the eyes), allergic salute (nasal crease), open-mouth breathing and facial grimacing due to itchiness. The nasal mucosa often appears oedematous and pale, with clear secretions (8).

There is a strong association with asthma, with up to 1/3 of the children with AR having asthma. Up to 80% of children with asthma have AR (4). This close link has been termed the United Airway Concept and is based on the fact that the upper and lower airways share similar epithelium and immunological mechanisms with an interaction between upper and lower airway inflammation. Even in the absence of clinical asthma, many children with AR have bronchial hyperreactivity (9).

Some studies have shown that treatment with intranasal steroids has a positive effect on asthma, and poorly controlled allergic rhinitis is associated with severe asthma (10, 11).

AR is considered a risk factor for the development of asthma.

The most common allergic triggers for AR include house dust mites, grass, weed and tree pollen, cat and dog allergens, and indoor and outdoor moulds. It is important for the management of AR to identify the allergic triggers for the child.

The presence of specific IgE, or a positive skin prick test does not necessarily mean that the allergen tested is the one triggering the symptoms. For example, a pollen allergic child may have positive specific IgE or skin prick test (SPT) to both grass and tree pollen, but only experience symptoms during the grass pollen season, making tree pollen sensitisation irrelevant and due to cross-reactivity with grass pollen allergens.

Therefore, a careful history of exposure and its relationship to symptoms is crucial.

For pollen-allergic children, it may be useful to monitor their symptoms over a season and correlate them with the amount and type of pollen concentration in the air. In some cases, component-resolved diagnosis may be helpful in distinguishing relevant from non-relevant sensitisation.

Sometimes allergy tests remain negative, despite a strong clinical suspicion of AR. In these children, local allergic rhinitis (LAR) should

be considered. This is a rhinitis phenotype characterised by the typical symptoms and history of AR, but with undetectable specific IgE to aeroallergens and negative skin prick tests, and a positive nasal provocation test (NPT) to one or more environmental allergens. The prevalence of LAR in children with chronic rhinitis is highly variable, ranging from 0-66% in different studies(12). Specific IgE has been detected in the nasal mucosa of 20-40 % of patients with a positive NPT, but the immunopathology remains unclear.

As a NPT is difficult to perform in children. The diagnosis of this condition is often made on clinical grounds and its response to treatment. The most common triggers are house dust mite, grass and tree pollen.

Other causes of rhinitis should also be considered. A differential diagnosis is given in Table 1. Referral to an otorhinolaryngologist may be warranted.

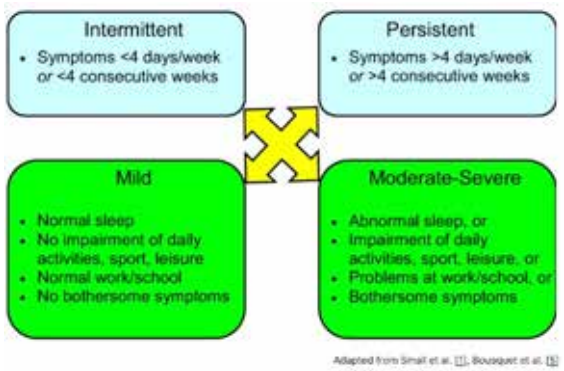
Allergic rhinitis is classified as intermittent or persistent, and in both conditions symptoms can be mild or moderate/severe symptoms (Figure 1). Treatment options vary according to this classification (2). A visual analogue scale is a useful tool to assess symptoms and monitor the effect of treatment.

Table 1: Differential diagnosis of allergic rhinitis in children.

Differential diagnosis of AR in children	
Non-allergic rhinitis	• Drug-induced • Hormone induced • Gustatory • Vasomotor rhinitis • Idiopathic • Gastro-oesophageal reflux
Infectious rhinitis	
Structural abnormalities: nasal septum deviation ; choanal atresia or stenosis	
Adenoid hypertrophy	
Immunodeficiency	• Hypogammaglobulinemia • Primary ciliary dyskinesia • Cystic fibrosis (nasal polyps)
Foreign body	
Benign and malignant tumours	
Cerebrospinal fluid leak	

Adapted from Differentiating Rhinitis in the Paediatric population by giving focus on medical history and clinical examination . Doulaptsi et al. Med Sci 2019;7(3):38

Figure 1: Classification of allergic rhinitis according to symptom duration and severity (Small P, Keith PK, Kim H. Allergic rhinitis. Allergy Asthma Clin Immunol. 2018;14(2_suppl):51).



Management of AR

A three-step approach is recommended for the management of allergic rhinitis.

Allergen avoidance, where possible, is the first step, followed by pharmacological treatment, and if indicated, allergen immunotherapy.

Allergen avoidance

Allergen avoidance is an effective strategy to control the symptoms of AR, but is difficult to achieve.

For house dust mites (HDM), the most important allergen is found in faeces of HDM. HDM feed on tiny flakes of human skin that are shredded mainly in bedding, carpets and curtains.

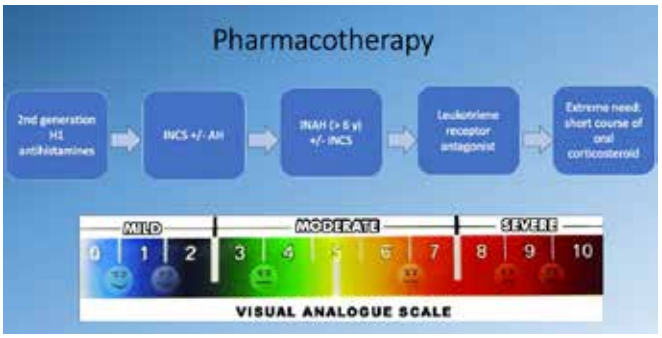
They thrive in humid conditions and are resistant to low temperatures. Washing at 40°C removes about 90%,of HDM allergens, while washing at 60 °C removes 100% of HDM allergens.

Measures to reduce the amount of HDM include the use of acaricides (chemicals that kill mites), impermeable mattress covers, frequent washing and cleaning, air filtration and vacuum cleaning with HEPA (High Efficiency Particulate Air) filters, removal of carpets and curtains and avoiding humidity.

Items that cannot withstand high temperatures, such as soft toys, can be frozen at a minimum of minus 15 °C for at least 16 hours, which will kill the house dust mites but does not remove the allergens (13).

Of all the measures, the use of acaricides appears to be the most effective, although multiple measures are needed to improve symptom control (Figure 2) (14).

Figure 2: Environmental control measures to reduce allergen levels and symptoms (Seidman MD, Gurgel RK, Lin SY, Schwarts SR, Baroody FM, Bonner JR, et al. Clinical Practice Guideline: Allergic Rhinitis. Otolaryngology-Head and Neck Surgery. 2015:152(1_suppl):S1-S43).



Pet allergens are present in saliva, urine and skin. There is no evidence for the existence of hypoallergenic animals, although there are differences in the amount of allergens shed by different breeds of dogs and cats. A study investigating the level of dog allergens in the home in so called hypoallergenic dogs compared with non-hypoallergenic dogs found no difference in the levels of dog allergens in the owner's homes (15).

Measures to reduce the level of pet allergens (frequent washing, vacuum cleaning with HEPA filters, avoiding animals in the bedroom) show a reduction in allergens but no effect on symptom scores.

Removal of the animal is the best option but compliance with this advice is often poor. Even if the advice is followed, it can take several months for the house to become allergen-free.

A study in 2010 showed that pet removal has a preventive effect on the secondary development of asthma (16).

Pollen allergen avoidance is difficult.

Keeping windows closed, staying indoors, taking a shower before bedtime, removing clothes from the bedroom, avoiding drying clothes

outdoors or staying indoors when the pollen count is high can be recommended. The Sciensano website (www.airallergy.be) provides useful information on the amount and origin of pollen in the air.

Pharmacological treatment (Figure 3)

Pharmacological treatment aims to control symptoms.

Treatment options vary according to the type (persistent or intermittent) and severity of symptoms. A step-up treatment plan is recommended with regular assessment of efficacy and adjustment according to symptom control. Patient preference should also be taken into account, for example in the choice of intranasal or oral therapy.

Several guidelines have been published (1-4).

Figure 3: Pharmacological treatment: stepwise treatment plan and visual analogue scale (AH = antihistamines, INCS = intranasal corticosteroids, INAH = intranasal antihistamines).

	Evidence Supports Reduction in Allergen Level		Evidence Supports Reduction in Symptoms	
Environmental Control Measure	**Yes**	**No**	**Yes**	**No**
Removal of pets	X		X	
Washing pets twice a week	X			X
Acaricides to kill dust mites	X		X	
Impermeable covers for bedding	X			X
Air filtration	X			X
Combined use of multiple control measures	X		X	

ANTIHISTAMINES

Second-generation antihistamines are often first line for mild to moderate symptoms, especially when sneezing, itchiness and runny nose are the main symptoms. They have a rapid onset of action and are therefore suitable for mild to moderate intermittent or persistent AR. Cetirizine, levocetirizine, loratadine and desloratadine are FDA approved for use from the age of 6 months.

Their safety and efficacy are well documented. Side effects are rare but include mild fatigue, headache, dizziness or gastrointestinal symptoms. There is no proven difference in effectiveness between the different antihistamines.

The use of first-generation antihistamines is no longer recommended in children because of their sedative properties with impact on cognitive function and their anticholinergic effects.

Intranasal antihistamines are more effective than oral antihistamines and start working within 15 minutes. They can be used from the age of 6 years. Many children do not like to use them because of the bitter taste. Epistaxis or headaches have been reported as side effects (3, 4).

INTRANASAL CORTICOSTEROIDS (INC)

Intranasal corticosteroids are the most effective treatment for AR with good effect on all nasal symptoms. They also improve symptoms of conjunctivitis. INC are the recommended treatment for moderate to severe, intermittent or persistent AR and are FDA approved from the age of 2 years. The onset of action is slow (5 to 12 hours) and clinical improvement usually takes several days. INC can be used alone as first-line therapy alone or in combination with an oral or intranasal AH.

Epistaxis or local irritation are common side effects. Long-term use does not cause damage to the nasal mucosa. Fluticasone propionate, fluticasone furoate, mometasone furoate and ciclosenide have minimal systemic absorption and are considered safe. No growth restriction has been documented with the use of these medications at the recommended doses, but growth monitoring is still recommended.

The duration of therapy is variable and is influenced by the child's allergic profile (intermittent vs persistent AR, intensity of the symptoms). When good symptom control is achieved, a step down in treatment should be considered.

OTHER THERAPIES

Irrigation with normal saline or mildly hypertonic saline has been shown to be a good adjuvant treatment (4).

In Belgium, leukotriene receptor antagonists are mainly prescribed for asthma. Although less effective than INC, their efficacy in mild to moderate AR has been demonstrated. In children with concomitant asthma, they can be a useful step-up treatment. It should be noted

Table 2: AIT studies in children.

Study (year)	Age	AIT Mode (Disease)	Duration	Clinical results	Immunological results
Des Roches et al. (1991)	Children	HDM SCIT (Rhinitis)	36 mos	↓ Occurrence in new sensitisation	-
Pajno et al. (2001)	Children	HDM SCIT (Rhinitis/Asthma)	36 mos	↓ Occurrence in new sensitisation	-
Möller et al. (2002)	Children	Grass and/or birch pollen SCIT (Rhinitis/Asthma)	36 mos	↓ BHR ↓ conjunctivitis VAS score ↓ asthma VAS score	-
Niggemann et al. (2006)	Children	Grass and/or birch pollen SCIT (Rhinitis/Asthma)	36 mos	↓ asthma Improvement in CPT	-
Valovita et al. (2011 & 2018)	Children	Grass SLIT (Rhinitis/ Asthma)	36 mos	↓ asthma symptoms ↓ medication use ↓ RTSS ↓ ICS	↓ total IgE ↓ Grass sIgE
Mosbech et al. (2014 & 2015)	Adolescent, Adult	HDM SLIT (Rhinitis/Asthma)	12 mos	↓ ICS	-
Nolte et al. (2016)	Adolescent, Adult	HDM SLIT (Rhinitis)	52 wks	↓ Total rhinitis SS ↓ Daily symptom and medications score ↓ VAS score	-
Okubo et al. (2017)	Adolescent, Adult	HDM SLIT	12 mos	↓ Total SS ↓ QoL	-
Masuyama et al. (2018)	Children	HDM SLIT	12 mos	↓ Rhinitis SMS	↓ HDM sIgE followed by decline ↓ HDM sIgG4

Abbreviations: BHR: bronchial hypersensitivity; CPT: conjunctival provocation test; ICS: inhaled corticosteroid; QoL: quality of life; RTSS rhinoconjunctivitis symptom score; SCI: subcutaneous immunotherapy; SLIT: sublingual immunotherapy; SMS: symptom and medication score; SPT: skin prick test; SS: symptom score; TNSS: total nasal symptom score; VAS: visual analogue scale.

that the FDA has warned against their use because of the possibility of neuropsychiatric adverse effects.

Topical and oral decongestants should be avoided because of their rebound effect and drug-induced rhinitis, although a short course of less than 10 days may be considered.

For severe, uncontrollable symptoms a short course (5 days) of oral corticosteroids is sometimes a last resort, but is not recommended due to its side effects.

Allergen immunotherapy (AIT)(5, 17)

Allergen immunotherapy is the only disease-modifying treatment.

It induces tolerance to the allergen by a shift in the immune system, with suppression of the Th2 responses, decreased production of IgE antibodies, increased IgG 4 antibodies and downregulation of mast cell and basophils. Modified allergens are administered subcutaneously (SCIT) or sublingually (SLIT). Safety and efficacy have been well demonstrated in adults. Although there are fewer studies in children, there is good evidence for pollen and HDM allergic children. An overview of studies exclusively in children is represented in Table 2.

There is no evidence for the use of AIT for other allergens in children. In adults, there is limited high quality evidence for AIT for cat allergy, no clear clinical evidence for dog allergy and low quality evidence for mould allergy (Alternaria).

The use of AIT can be considered in children from 5 years of age with moderate to severe AR with or without asthma and with insufficient symptom control on pharmacological treatment. The recent GINA guidelines have included AIT as an adjuvant treatment option for children with asthma allergic to HDM.

AIT is currently not reimbursed in Belgium.

Short-term beneficial effects are noticeable 2-4 months after starting AIT, with significant improvement in symptom control and a reduction in medication use in 60-85% of the patients.

Long lasting beneficial effects have been demonstrated in the GAP study, with effects on both AR and asthma symptoms 2 years after treatment with SLIT in children allergic to grass pollen (18, 19). The PAT study showed reduction in symptoms in grass and /or birch pollen allergic children up to 10 years after treatment with SCIT as well as a reduction in new development of asthma.

There is currently good evidence for the prevention of asthma in pollen-allergic children for up to 2 years after treatment. For other allergens, such as house dust mite, there is insufficient evidence of a beneficial preventive effect on asthma.

There is insufficient evidence that AIT has a preventive effect on the development of new allergic sensitisations (20).

The choice between the sublingual and subcutaneous route depends mainly on patient preference. There is insufficient evidence to suggest that the latter is more effective than the former. The duration of treatment for both therapies is 3-5 years. SCIT starts with weekly up-dosing, followed by 2-weekly injections for 2 months, then monthly injections, although up-dosing schedules may vary between different products. Local reactions at the injection site (redness, swelling, itchiness) are common (50%). Systemic reactions are rare (0.1%) but is important that the child is observed for 30 minutes and that rescue medication (adrenaline, antihistamine) is readily available (17).

Risk factors for systemic reaction in AIT are uncontrolled asthma, intercurrent infection, a high degree of sensitisation, vigorous exercise after injection, poor compliance, mast cell disease and the use of beta blockers.

SLIT needs to be administered daily and therefore requires good compliance. Common side effects include itchiness in the mouth, swelling of the tongue or lips. Systemic reactions are rare, but it is recommended to give the first dose under supervision. The success of AIT depends mainly on the child's allergic profile, the choice of the right allergens and compliance to therapy. It is possible to combine several allergens at the same time, such as grass and tree pollen. HDM and pollen allergens cannot be mixed, due to degradation of the allergen by enzymatic activity. They should be administered at different injection sites or, in the case of SLIT, at different times.

Contraindications to immunotherapy include severe asthma, active autoimmune disease, malignancy and poor compliance to therapy (5, 17).

Conclusion

AR is a chronic condition with a significant impact on quality of life, and a risk factor for the development of asthma.

Management consists of allergen avoidance, pharmacotherapy and allergen immunotherapy. AIT may be considered in children from 5 years of age with AR and a documented and relevant sensitisation to pollen and/or house dust mite with moderate to severe symptoms despite adequate pharmacotherapy. It may also be considered for the prevention of asthma in pollen-allergic children.

When deciding between the different treatment options, patient and family's preferences should be take into account.

Conflicts of interest

The author has no conflicts of interest in relation to the subject matter of this manuscript.

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