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Current management of allergic rhinitis in children

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Over the last 20 years, there has been significant progress in our understanding of the pathophysiology of allergic rhinitis, including the discovery of new inflammatory mediators, the link between asthma and allergic rhinitis ('one airway–one disease' concept) and the introduction of novel therapeutic modalities. These new insights have been documented in the Allergic Rhinitis and its Impact on Asthma guidelines and have led to the creation of evidence-based management algorithms. We now understand the importance of a common strategy for treating allergic inflammation of the upper and lower airway as a way of improving outcome, reducing hospital admissions, providing better quality of life and perhaps, altering the natural course of the 'allergic march'. A therapeutic ladder is suggested: Whereas for mild intermittent allergic rhinitis, allergen avoidance should be the first line of treatment with subsequent addition of a second generation topical or oral antihistamine, nasal saline or cromoglycate, in cases of moderate to severe allergic rhinitis, a nasal steroid is the treatment of choice. If a patient with moderate/severe persistent allergic rhinitis fails to improve after 4 wk of adequate treatment, patient compliance or the diagnosis must be re-assessed. In such cases, when the diagnosis is in doubt, a careful clinical examination including nasal endoscopy is mandatory to assess for other potential causes of nasal obstruction. In children who suffer from concomitant allergic rhinitis and asthma, a management algorithm that addresses concurrently asthma and allergic rhinitis is vital, both from a theoretical and from a practical point of view: Parents overwhelmingly prefer a single strategy for the treatment of their child's upper and lower airway symptoms; however, the overall quality of life in children with severe asthma can be significantly improved if rhinitis is adequately addressed.

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Arguably, one of the most important public health issues in the Western countries over the last few decades has been the alarming increase in the prevalence of allergic conditions, including allergic rhinitis, in children (1). However, this development has been accompanied with significant progress in our understanding of the pathophysiology of allergic rhinitis, including the discovery of new inflammatory mediators, the link between asthma and allergic rhinitis ('one airway–one disease' concept) and the introduction of novel therapeutic modalities. These new insights have been documented in the Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines (2) and have led to the creation of evidence-based management algorithms. We now understand the importance of a common strategy for treating allergic inflammation of the upper and lower airway as a way of improving outcome, reducing hospital admissions, providing better quality of life and perhaps, altering the natural course of the

'allergic march' – more so in children, where it may be linked to primary and/or secondary prevention. As new modalities of treatment (sublingual or subcutaneous immunotherapy, anti-IgE) are introduced, we gradually acquire a better understanding of their place in the therapeutic armamentarium, alongside pharmacological management (3), allergen avoidance (4) and complementary therapies (5). The management of allergic rhinitis in children tends to follow the same rationale as that in adults; however, there are specific considerations in children that need to be taken into account. There is in general less evidence regarding the efficacy of various treatments, such as immunotherapy, in children (6, 7), whereas other forms of treatment, such as oral steroids, although effective, have a different risk-benefit profile in children compared with that in adults.

Case 1

Marie was 14 years of age when she first noticed that she had a problem with 'summer colds'. As the symptoms were not so bad, she did not seek treatment. She was fine throughout the winter. Next summer, she was revising hard for her examinations when the colds began again. This year they were worse; she had a continuous runny nose, sneezed and had itchy, red eyes.

Being a teenager, she did not seek adult advice but asked her friends, who told her that she probably had hay fever and suggested that she buy some medicine from the local pharmacist. The pharmacist suggested an oral antihistamine and was given chlorphenamine, as she asked for the cheapest one. She started taking one tablet at night as directed. Unfortunately, although her nasal and eye symptoms improved, she found it hard to get up in the morning and was drowsy during the day. Her results were poorer than expected and provoked an enquiry from her teachers. One of them suggested that Marie should see her primary care provider about hay fever so that the problem could be solved before Marie's important examinations the following summer. Marie's doctor took a history and found that her symptoms began in May and continued until the end of July – the typical grass pollen season in the UK. She noted that Marie's eyes and nose were affected and that her worst symptoms were rhinorrhoea and itching. As the symptoms occurred for more than 4 days at a time and for more than 4 wk, Marie's condition was classified as persistent rhinitis; because her schooling was affected, it was classified as moderate to severe. The following year, Marie began using a topical nasal corticosteroid plus a non-sedating antihistamine in early May. She used both every day until the end of July and hardly noticed any hay fever symptoms. She did very well in her examinations.

Discussion

Up to one-third of children with allergic rhinitis (AR) are never seen by a doctor, and the majority of children with moderate to severe symptoms are undertreated (8), despite the fact that allergic rhinitis may have a significant impact on a child's everyday activities and quality of life (9). In such cases, inappropriate self-management may include the use of sedating antihistamines, which are contraindicated in the treatment of AR, as they tend to exacerbate the deficits in cognitive functioning and school performance, which are frequently associated with moderate to severe allergic rhinitis: A teenager using these has a 70% chance of dropping a grade in one subject at GCSE compared with their mock examination grade (10).

Classification of rhinitis according to the ARIA guidelines is helpful in choosing the appropriate modality of treatment: Allergic rhinitis has been historically divided into perennial (indoor allergens and symptoms present year-round) and seasonal (outdoor allergens and symptoms having a strong seasonal variation); however, this division is not satisfactory: Many patients are sensitized to both indoor and outdoor allergens, and their symptoms may be present during the whole year, with seasonal exacerbations. On the other hand, whereas patients with perennial allergic rhinitis may have symptoms that do not interfere with their everyday life, patients with seasonal rhinitis may suffer significant morbidity. Thus, the new subdivision classifies patients along two axes: duration of symptoms (persistent or intermittent) and severity of symptoms (mild or moderate/severe). Symptoms present for more than 4 days/wk and for more than 4 wk are diagnostic of persistent allergic rhinitis (PAR), whereas the presence of symptoms that significantly impair sleep or daily activities, work or study classifies a patient as suffering from moderate or severe AR (11). The need for the new classification is exemplified in the history of this patient – seasonal allergic rhinitis is not necessarily intermittent and is often not mild: Marie was suffering from persistent (more than 4 days/wk and more than 4 wk/yr), moderate/severe (symptoms affecting school performance) allergic rhinitis. According to the ARIA guidelines, topical

corticosteroids are the first-line therapy for such patients, with an additional non-sedating antihistamine if needed. It is also recommended that treatment is initiated 1–2 wk before the onset of symptoms and medications are taken regularly rather than on an as-needed basis. A therapeutic ladder is suggested: Whereas for mild intermittent allergic rhinitis, allergen avoidance should be the first line of treatment with subsequent addition of a second generation topical or oral antihistamine, nasal saline or cromoglycate; in cases of moderate to severe AR, an intranasal steroid is the treatment of choice. In these patients, topical or oral antihistamines can be used *in addition to* nasal steroids, although there is no evidence of higher efficacy of this combination of treatment than that of a nasal steroid alone. When the nose is heavily blocked for short periods of time (up to 10 days), a nasal decongestant may be helpful, although its efficacy is limited in nasal obstruction and it has no effect on rhinorrhoea, nasal itching or conjunctivitis (Fig. 1). Generally, intranasal steroids are more effective than antihistamines (12) and it has been shown that the use of new, selective formulations with less bioavailability is not associated with growth retardation or any other significant systemic side effects in children (13, 14). Cromoglycate is probably the medication with the best safety profile in children; however, it is less effective than either antihistamines or nasal steroids and there are compliance issues related to its need for frequent administration. The use of subcutaneous or sublingual immunotherapy, although promising as a potential way to 'halt the allergic march', cannot be currently recommended as a standard treatment: Evidence regarding its efficacy in children is still inconclusive and significant uncertainty persists regarding the recommended dosing schedule, treatment

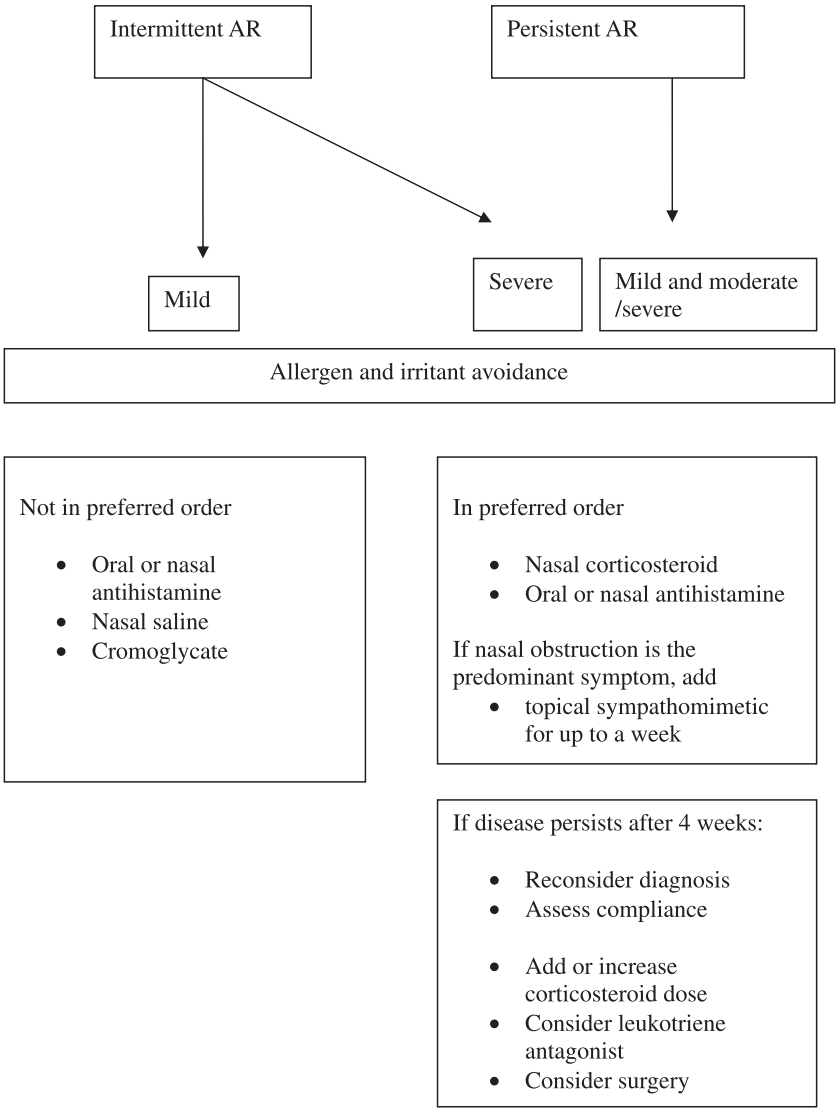

Fig. 1. Management algorithm for allergic rhinitis in children.

duration and side effects (6, 7). However, in situations where medical treatment fails, immunotherapy can be considered. Oral steroids are generally not indicated in children with allergic rhinitis, whereas ipratropium nasal spray is not licensed for use in children of less than 12 yr of age.

Case 2

A 5-yr-old boy with a long history of blocked nose and asthma was brought to the clinic by his mother. He described a continuous mucopurulent nasal discharge, associated with nasal obstruction and snoring. Although he did not demonstrate any specific reactivities on SPT, he has been provisionally diagnosed with AR and has been provided with a nasal steroid spray and oral antihistamines. Both he and his mother were keen to point out that he has been taking his medications scrupulously for the last 3 months, with no evidence of any benefit. He also had a wet cough, for which his doctor had prescribed two inhalers: one containing corticosteroid, the other salbutamol. These were rarely used as they did not improve his symptoms. He was otherwise well and had no past history of eczema. There was no family history of atopy, except that a cousin had similar symptoms.

Examination revealed a slight boy on the 10th centile for weight and height, who was breathing through his mouth. There was a thick white discharge present in both nostrils, with swollen pale inferior turbinates. His chest was indrawn in the lower intercostals area and there were one or two wheezes audible on auscultation. Nasal endoscopy of the nose after decongestion and suctioning revealed the presence of bilateral nasal polyps. A chest X-ray showed evidence of areas of infiltrate and atelectasis bilaterally. A sweat test (quantitative pilocarpine iontophoresis test) was organized which suggested the diagnosis of CF, which was also confirmed with genetic testing. Following application of a topical decongestant and anaesthetic and under endoscopic guidance, cultures were obtained from middle meati of the maxillary sinuses. On the basis of cultures and sensitivity testing, he was placed on a long-term course of systemic antibiotics and instructed how to perform daily nasal irrigation, with good response.

Discussion

Allergic Rhinitis and its Impact on Asthma guidelines (Fig. 1) state that if a patient with moderate/severe persistent allergic rhinitis fails to improve after 4 wk of adequate treatment, either patient compliance or the diagnosis must be re-assessed. The young boy in this case had been receiving nasal steroids and antihistamines for a few months and failed to show any signs of improvement – suggesting that he was either non-compliant or misdiagnosed. In such cases, when the diagnosis is in doubt, a careful clinical examination including nasal endoscopy is mandatory. In this young boy, the presence of polyps led to the diagnosis of cystic fibrosis (CF), a condition that (like primary ciliary dyskinesia) may be easily confused with chronic rhinitis/rhinosinusitis with asthma (15). However, other causes of nasal obstruction in children which need to be excluded include enlarged adenoids, deviated nasal septum and benign or malignant nasal tumours. In all of these cases, nasal endoscopy is very helpful and can almost always be performed in children, provided that a clear explanation of the procedure is given, appropriate local anaesthesia is applied and a gentle technique is used (16).

Although most patients with cystic fibrosis are diagnosed in infancy or early years of childhood, in some cases the diagnosis may be delayed until adolescence or even adult life. Approximately one-third to half of the children with CF present with nasal polyps (17). Nasal polyps are rare in children and their presence should always alert the examining doctor to the possibility of CF – indeed, in a recent study of children undergoing endoscopic sinus surgery for nasal polyposis, the majority of children with nasal polyps had cystic fibrosis (18).

The most significant breakthrough in the management of CF has been the use of long-term antibiotics (including intravenous) with aim of eradicating bacteria colonizing the airways rather than short pulses of oral antimicrobials used only in exacerbations (19). This has led to significant improvements in the control of these patients' respiratory symptoms as well as their overall life expectancy, and together with oral and nasal steroids, the use of regular saline nasal douching forms the cornerstone of medical management of the nasal manifestations of CF.

Case 3

An 8-yr-old boy was seen in the allergy clinic with difficult to control asthma and rhinitis. His general practitioner had prescribed him a steroid inhaler that he had been using intermittently and a beta mimetic inhaler that he had been using on an as-needed basis. He had attended accident and emergency twice over the last 6 months with

acute exacerbations of his asthma, missing 12 days from school, and had also had two short courses of oral steroids. He had been trying allergen (house dust mite) avoidance measures and had also undergone a year of sublingual immunotherapy, with limited results. During the interview, his mother also mentioned his nasal symptoms, notably his constant snuffling, sneezing and permanent runny nose. There was a family history of atopy, as his older sibling had eczema and his mother was suffering from asthma. Examination showed that the boy breathing through his mouth and was constantly rubbing his nose, with a resultant allergic crease on the dorsum of his nose. Examination revealed a significantly reduced nasal airway, an abundance of clear watery secretions and pale oedematous inferior turbinates. On auscultation, he had multiple bilateral wheezes and slightly reduced air entry. His FEV1 was 65% of that predicted for his age and rose to 85% after bronchodilation, while the skin prick test revealed a strong positive reaction to house dust mite.

He was started on a new generation nasal steroid with low bioavailability, an oral leukotriene receptor antagonist and an inhaled steroid, with the adrenergic inhaler to be used on an as-needed basis. Reassurance was provided regarding the systemic side effects of intranasal and inhaled corticosteroids and it was explained that he should receive combined treatment for his allergic rhinitis and asthma. At a follow-up appointment, 2 months later, he was much better, with no days off school and no further accident and emergency attendances. The dose of inhaled steroid was lowered and a further follow-up was arranged at 3 months.

Case 4

A 10-yr-old boy was referred to an allergist by his paediatrician, who had been treating the boy for rhinoconjunctivitis and asthma since he was 7-yr old. His medication consisted of inhaled steroids and antihistaminics on a daily basis and a short-acting beta agonist as needed. His mother said that he had nasal and ocular symptoms all year-around, with exacerbations during spring and summer, and that provocation with dust and cat also led to worsening of the symptoms. His earlier blood results showed specific IgE to house dust mite, grass pollen, tree pollen, cat and dog. Although he used his medication according to prescription, a recent long function test showed a reversibility of 16%. At the first visit, his mother told that the boy had problems at school, showed behavioural problems when allergic symptoms were bad and also had difficulty in playing football, which he loved, because of his asthmatic symptoms. As the boy fulfilled the criteria for persistent, moderate severe rhinoconjunctivitis, a nasal steroid was started together with antihistaminic eye drops, because of very troublesome eye symptoms. After consultation with his paediatrician, the inhaled steroids were replaced by a combination of long-acting beta agonists and an inhaled steroid. The daily use of antihistaminics was continued. Under this regimen, the symptoms improved but were not completely controlled, even after adding a leukotriene antagonist. The option of immunotherapy was discussed with the parents and the boy, as a measure to improve symptoms as well as the potential side effects, including anaphylaxis. In the autumn, the boy was started on subcutaneous immunotherapy with tree pollen, grass pollen and house dust mite. Next spring and summer, the symptoms were well-controlled, even after reducing his medication; he hardly used the short-acting beta agonist, stopped the leukotriene antagonist and used the oral antihistaminic on an as-needed basis instead of daily. Furthermore, his behavioural problems diminished, he found his school work much easier and – most important to the boy himself – his soccer game had much improved.

Immunotherapy in children is still a matter of debate. Whereas some advocate the use of immunotherapy at an early stage to prevent polysensitization and asthma (20), others point out that the evidence for the effect of immunotherapy in children is lacking (21). Furthermore, the evidence for treating patients with multiple allergen immunotherapy is even more limited (22), although in the Netherlands allergists do treat patients with multiple allergens with satisfactory results. With regard to the treatment with immunotherapy, according to the ARIA guidelines, the indications for immunotherapy are the same in both adults and children: (i) symptoms are predominantly induced by allergen exposure; (ii) prolonged season or symptoms induced by succeeding pollen seasons; (iii) rhinitis and symptoms of the lower airways during peak allergen exposure; (iv) antihistamines and moderate dose topical steroids insufficiently control symptoms; (v) patient does not want to be on constant or long-term pharmacotherapy; (vi) pharmacotherapy-induced side effects (23). In this case, despite optimal therapy, the boy still had troublesome symptoms; therefore, the option of immunotherapy was discussed with both parents and the child. In this particular

case, this proved to be a good choice. However, there are disadvantages that need to be discussed: Immunotherapy is a long-term investment as it needs to be performed for at least 3 yr. Furthermore, there is the risk of side effects, in both SCIT and SLIT. In this case, SCIT was chosen because we felt that the evidence for SCIT, and especially its long-term results, was, and still is, more robust than that for SLIT. SCIT has the disadvantage that the patient has to attend the practice to receive his allergy shots, whereas SLIT demands significant discipline from the patient or the parent to guarantee adherence to the management schedule. Moreover, the required 30-min wait after the injections in the practice means that professional help is available, should complications occur, whereas SLIT is taken at home where adequate help in case of complications is not guaranteed. Should one choose for SLIT, this potential risk has to be discussed with the parents thoroughly. Although the effect of immunotherapy in asthma has been assessed in a Cochrane review in 2003, special attention needs to be paid to patients with asthma starting immunotherapy. As stated in the ARIA guidelines, patients with severe pulmonary disease should be excluded. Furthermore, it is advised to monitor pulmonary function by peak flow measurement. In our own practice, in both adults and children with asthma, a long function test is performed before starting immunotherapy to ensure that FEV1 is at least 70% of that predicted and that there is no or only mild bronchial hyper-reactivity.

In conclusion, immunotherapy can be a good choice in children with troublesome symptoms despite adequate treatment, but pros and cons need to be discussed with both the caretakers and the patient.

Discussion

The original as well as the update on the ARIA guidelines have stressed the link between allergic rhinitis and asthma (24, 25). It is now well-established that allergic rhinitis is one of the strongest risk factors for asthma and that children who suffer from asthma and concomitant allergic rhinitis tend to have a much worse quality of life, more difficult to control asthma and up to 2.5 times more frequent asthma-associated hospital admissions (26, 27). From a pathophysiological point of view, there is clear evidence of a common allergic pathway (28): Nasal allergen challenge results in increased nonspecific bronchial responsiveness (29) and vice versa, whereas segmental bronchial provocation in patients with AR but no asthma results in allergic inflammatory changes in the nose (30). However, although the link is well-established, a causal relationship is not – and it is possible that AR and asthma are both manifestations of an underlying systemic allergic tendency (31). In any case, the epidemiological, if not causal, association between these two conditions renders the assessment of children with AR for asthma and vice versa mandatory. A management algorithm that addresses asthma and allergic rhinitis simultaneously is crucial, both from a theoretical and from a practical framework: Parents overwhelmingly prefer a single strategy for the treatment of their child's upper and lower airway symptoms; however, the overall quality of life in children with severe asthma can be significantly improved if rhinitis is adequately addressed. Studies assessing whether more effective treatment of AR improves the outcome of asthma have been mostly observational, not randomized, and have not been conclusive (32). However, a recent nested case–control study showed that in patients older than 6 yr with severe asthma, treatment of allergic rhinitis with nasal steroids or antihistamines is associated with reduced hospital admission rate (odds ratio 0.37) and reduced use of accident and emergency service (odds ratio 0.22) (33). Although it is hoped that further studies will elucidate the link between allergic rhinitis and asthma in the future, a common strategy for their treatment is currently amply justified on the basis of available evidence. Regarding the use of immunotherapy in children, studies with both SCIT and SLIT are needed to further elucidate their role in both symptom improvement of rhinitis and asthma, and in the prevention of polysensitization and asthma.

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MCQ's for allergic rhinitis in children [correct answers in bold font]

Question 1:
According to the new ARIA classification, a 12-yr-old boy who has rhinitic symptoms 5 days/wk for May and June, which interfere with his school progress, suffers from:

A. Mild seasonal allergic rhinitis
B. Moderate to severe intermittent allergic rhinitis
C. Mild persistent allergic rhinitis
D. Moderate to severe persistent allergic rhinitis

Question 2:
In a 7-yr-old boy suffering from moderate to severe persistent allergic rhinitis, who does not respond to allergen avoidance, the next line of treatment should be

A. Oral steroids – 1 mg/kg for 7 days
B. Non-sedating second-generation antihistamines – 5 mg od
C. Nasal steroids (low bioavailability formulations)
D. Intramuscular steroid injections

Question 3:
John is 5-yr-old boy and has been using nasal steroids for the past 2 months for his allergic rhinitis, with no improvement. What would you do next?

A. Perform a CT scan of the sinuses
B. Prescribe and administer intramuscular steroid injections

C. Reassess compliance and the diagnosis – including performing a nasendoscopy

D. Add cromoglycate

Question 4:

Among children who have asthma, which of the following statements is true?

A. 2–4% of them also suffer from rhinitis.

B. Children who receive adequate treatment for their rhinitis tend to have fewer admissions for their asthma.

C. Children who suffer from concurrent rhinitis tend to have milder and easier to control asthma.

D. There is convincing evidence that rhinitis is an aetiological factor for asthma.