

LITERATURE REVIEW

Allergic diseases in adolescents

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ABSTRACT

OBJECTIVES. We reviewed the literature on allergic disorders during adolescence.

MATERIAL AND METHODS. The Pubmed, Google, Google Scholar and Proquest Central databases were used with search terms: adolescent, teenager, allergic rhinitis, asthma, atopic dermatitis and food allergy.

RESULTS. Children with a proven allergy have a risk for developing another allergic disorder that is 8-fold higher compared to normal and approaching 7-fold for asthma. The age at which allergy is diagnosed in childhood has a powerful bearing on whether allergic disorders or asthma develop in adolescence. Atopic response severity in a patient during childhood predicts the severity of allergic asthma as an adult. Patients may become asthmatic as adolescents, probably due to a late presentation of allergic disease, or as the presenting complaint for the triad of intrinsic asthma, nasal polyp formation and aspirin intolerance (so-called Samter triad). Allergic eczema (Atopic dermatitis) carries on into their adolescent years in between 10 and 20% of children. Food allergy (FA) is more frequently noted in childhood and adolescence than in adulthood. For the most part, symptoms were attributable to pollen-associated FA and of mild severity. Being hypersensitive to food for non-allergic reasons was rarer.

CONCLUSION. Allergic rhinitis represents a significant risk factor for becoming asthmatic, whether in childhood, adolescence or adulthood. Atopic dermatitis and food allergy are also frequent conditions during adolescence. Pollen-associated FA constitutes an important part of the food allergy. Furthermore, food allergy may be the leading trigger for anaphylaxis. Common associations/comorbidities of atopic dermatitis reported are other atopic conditions such as food allergies, asthma and allergic rhinitis/rhinoconjunctivitis.

KEYWORDS: allergy, adolescent, allergic rhinitis, asthma, food allergy.

INTRODUCTION

Allergy represents a pathological response of the immune system to a stimulus that typically is innocuous to most humans. Allergy results in the immune system treating the harmless substance as harmful. The substances which cause allergy are typically dust, food items, pollen of plant origin, or medications, to which antibodies are raised. There are also cellular responses involving the secretion of immune mediators, such as histamine. Histamine release accounts for the symptomatology of allergic responses within the nasal cavity, eyes, cutaneous system, respiratory system and gut. Once a response has been triggered initially, subsequent exposure to the epitope provokes a broadly similar immune allergic response¹.

Allergy may be manifested through a wide range

of reactions, progressing in severity from mild rhinorrhoea to severe dyspnoea. In adolescence, cases of asthma may present with allergic responses to cold. Somewhat unusually, allergy may progress to anaphylaxis, with attendant threat to life. Anaphylaxis is characterised by dyspnoea, dysphagia, lingual, labial and pharyngeal oedema and vertigo and may happen at any point up to four hours after contact with an offending allergen¹.

How allergic diseases develop, and what features they present with, depends on many different factors, relying, as it does, on complex interactions between genes, the presence of the allergen in the environment and more general factors like smoking status and the presence of infections. Allergic prophylaxis entails the necessity of keeping clear of the offending allergen, whilst also taking into account the various

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medications for use in the general population, children at first allergic presentation or in the chronic phase of the disease, and infants in whom the allergic response presents a severe risk of recurrence².

MATERIAL AND METHODS

This review covers allergic diseases during adolescence. The Pubmed, Google, Google Scholar and Proquest Central literature databases were queried from Kırıkkale University, using the following search terms: adolescent, allergic rhinitis, asthma, atopic dermatitis and food allergy.

Clinical trials were included in searching Pubmed, whilst articles in which allergic diseases in adolescence were not a central theme, or previous reviews, were discounted. The search covered the literature from the period 1982 onwards.

Searching using the terms “adolescent”, “teenager” and “allergic rhinitis” in combination caused 6,822 papers to be retrieved, from which 1,547 met the inclusion criterion of reporting on a clinical trial. 1,514 of these papers were then excluded, as they mainly concerned a different theme or were themselves review articles, leaving 33 papers to consider.

Searching using the terms “adolescent”, “teenager” and “asthma” in combination allowed 30,278 papers to be retrieved, from which 4,856 met the inclusion criterion of reporting on a clinical trial. 4,780 of these papers were then excluded, as they mainly concerned a different theme or were themselves review articles, leaving 76 papers to consider.

Searching using the terms “adolescent”, “teenager” and “atopic dermatitis” in combination allowed 4,952 papers to be retrieved, from which 684 met the inclusion criterion of reporting on a clinical trial. 670 of these papers were then excluded, as they mainly concerned a different theme or were themselves review articles, leaving 14 papers to consider.

Searching using the terms “adolescent”, “teenager” and “food allergy” in combination allowed 4,091 papers to be retrieved, from which 419 met the inclusion criterion of reporting on a clinical trial. 412 of these papers were then excluded, as they mainly concerned a different theme or were themselves review articles, leaving 7 papers to consider.

RISK FACTORS FOR ALLERGIC DISEASE DURING ADOLESCENCE

Adolescents who had an allergy diagnosed during childhood are known to be at increased risk of allergic disease or asthma. Kaila et al. report that a confirmed allergy between the ages of 9 and 18 months

(although not clinical suspicion on its own) was predictive of allergy at the age of 12 or 15 years. It did not predict the development of asthma, however³. For children in whom allergy is confirmed, subsequent allergic disease as adolescents was 8-fold more common than in those without such an allergy, and subsequent asthma was 7-fold likelier. Hence, the timing of allergy formation has a powerful bearing on subsequent allergic or asthmatic disease in adolescence. The severity of atopic response in the child powerfully influences how allergic asthma subsequently develops in the adult^{4,5}. For children under 2 years old, allergies are suspected in approximately 14%, but at age 5, 1% have a suspected only and 9% an actual confirmed allergy³.

Symptoms involving breathing occur with greater frequency in those patients who have received a diagnosis of (severe) atopy as young children than in those whose allergic response was less severe or developed at an older age⁶⁻⁸. There is a complex matrix of risks governing if and for how long allergy or asthma occurs⁹ and this renders ascertaining the likely prognosis in adulthood for children with atopy or asthma significantly difficult^{3,10,11}.

Worldwide, the highest incidence of allergic dermatitis recorded in early childhood is found in Finland, at 15-20%¹². Cutaneous allergic symptomatology occurs even more frequently, reaching 80%¹³. There is a paucity of data relating to long term follow-up of children with allergic conditions into adulthood, and what exists compromises for the most part prospective studies with a limited follow-up of only 2 to 3 years. It is thought that food allergies may be found in 1 in 3 children under the age of two, a surprisingly high number¹⁴. Milk allergy, food allergy and allergic conditions in early childhood occur at a rate of 2%^{15,16}, 8%¹⁷ and between 13 and 17%¹⁸, respectively. For young adults, the risk of atopy is put at 1/3¹⁹. Some 3-7% of adolescents are asthmatic, with the same numbers again having some symptoms suggestive of asthma, according to research undertaken in Finland that followed up cases until the age of 32²⁰.

ALLERGIC DISEASES IN ADOLESCENCE

Research undertaken in Norway into how common asthma, hay fever and allergic dermatitis affect schoolchildren aged 7 to 14 looked at rates from 1985 to 2008 and found that the prevalence of hay fever was rising, whilst that of allergic dermatitis remained steady²¹. Similar research done in England with schoolchildren aged 7 to 12 found that wheezing was becoming less common, whilst allergic dermatitis and rhinoconjunctivitis were on the rise^{22,23}.

The Brazilian ISAAC (International Study of Asthma and Allergies in Childhood) study revealed that asthma in children aged 6 to 7 rose from a prevalence of 21.3% in the Phase 1 study (ISF1) to a prevalence of 24.4% in Phase 3 (ISF3). Rhinoconjunctivitis and allergic dermatitis showed no change. The rates were 12.5% and 12.0% for rhinoconjunctivitis, and 6.8% both times for allergic dermatitis. The following allergic disorders became less common amongst atopic disorders: symptoms of asthma (from 22.7% to 19.9%); rhinoconjunctivitis (from 16.2% to 15.8%); allergic dermatitis (from 5.3% to 4.2%)^{23,24}.

Asthma in adolescence

Adolescents' daily existence is markedly affected by chronic conditions, such as asthma²⁵. Indeed, one in three cases of asthma in this cohort report having panic disorder or anxiety problems^{26,27}.

Whilst research has already shown that asthma has been becoming more prevalent in children and adolescents alike over the last 20 years, in more recent times, researchers have focused on epidemiological features of asthma in adolescents. Anderson et al., reporting on the British arm of ISAAC²⁸, noted an approximately 20% decrease in self-report of symptoms of asthma amongst 13- and 14-year-olds, over the period 1995-2002. Swiss adolescent cases of asthma, allergic hypersensitivity and allergic rhinitis did not increase in number over the period 1992-2000²⁹, nor did those in Italy between 1994 and 2002^{25,30}. Asthma has a predilection for males in early childhood but becomes less frequent following puberty³¹.

Epidemiological researchers have ascertained that close to 80% of childhood cases of asthma are asymptomatic after puberty has been passed through³². A cohort study with a prospective methodology that looked at schoolchildren in Australia every 7 years until they became adults found that, whilst being diagnosed with wheezing bronchitis was associated with only moderate breathing problems in adolescence and adulthood, being asthmatic entailed ongoing problems with wheeze and constricted airways³³. Despite this, whilst at age 14 lung function was markedly deficient, such a situation did not persist into the adulthood²⁵.

How asthma changes for adolescents might be attributable to the changing environmental conditions that adolescents experience, not forgetting activities adolescents, rather than children, engage in. The risk of severe asthma may rise on account of multiple circumstances, for example smoking (whether actively or passively), being indoors for longer periods, alterations in nutrition, alcohol misuse and being more exposed to chemical hazards²⁵. For children in particular, passive smoking is accompanied by wors-

ening asthma grade and symptomatology and deteriorating pulmonary function³⁴.

The UK has around 800,000 or more teenaged cases of asthma, yet the diagnosis and management of the condition is frequently sub-optimal. Rates of adolescent asthma and associated impairments are at least at the level of younger cases, but low concordance with medication in this group not infrequently causes symptoms to be under-controlled and results in excess morbidity³⁵. In these children, the wheezing prevalence and the level of lung function impairment are generally established by the age of 6 and seemingly do not change significantly up to the age of 16³⁶.

When asthma begins in adolescence, it is typically the result of a late developing allergy³⁷ or the presenting complaint for the Samter triad³⁸.

Allergic hypersensitivity and hyper-responsive airways are described as risk factors for becoming asthmatic, the situation becoming chronic and higher-grade asthmatic disease in both adolescents and younger adults²⁵. The chronicity of asthma in adolescents as revealed by different presentations of wheezing in adolescents is associated with various comorbid conditions in early childhood, especially with rhinitis, both allergic and non-allergic types³⁹. Allergens that persist all year through (e.g., mites) are a major determinant of asthma becoming persistent⁴⁰, with the impairment in lung function having a knock-on effect on how the lungs grow over time⁴¹. Intriguingly, whilst mothers who have an allergic history are at risk of having offspring of either sex who wheeze in childhood, this risk only applies to female offspring once adolescence is reached⁴².

This apparent sex bias may be a result of various factors, such as endocrine alterations⁴³, sex-linked differences in the way the airway grows and works⁴⁴, gender lifestyle variations⁴⁵, psychosocial factors including males' proclivity towards underplaying their symptoms⁴⁶, or a systematic anti-female bias in the way illness is diagnosed and managed in society (so-called Yentl Syndrome)⁴⁷.

Girls who develop obesity in late childhood have a probable risk of new onset asthma between the ages of 11 and 13, especially where the onset of puberty was early⁴⁸. Whilst such an observation powerfully corroborates the extent of endocrine involvement in asthma, how precisely this occurs and how obesity and asthma interact remains unknown^{43,49}.

Diagnosing asthma in adolescents is rendered more difficult as a result of various circumstances. Adolescents usually deny they have symptoms of asthma, much as occurs with other conditions in this age group. Unsurprisingly, this results in situations like the research showing that, where

screened by history and spirometry, approaching 30% of teenage athletes were given a new diagnosis of exercise-induced asthma⁵⁰.

Allergic rhinitis in adolescence

Allergic rhinitis (AR) involves both early and late inflammatory responses in the mucosa of the nose, occurring through IgE⁵¹⁻⁵³, to a variety of allergens, such as house dust mite, pollen, domestic animal dander and moulds⁵⁴. It is frequent in children and adolescents²⁴ and gives rise to persistent symptomatology with concomitant impairment of psychosocial functioning and scholastic performance⁵⁵⁻⁵⁷. AR occurs at rates ranging from 1.4% to 39.7%, with wide geographical variation^{58,59}.

There are both environmental (smoking, polluted air, infective agents, dietary) and genetic influences on the genesis of AR. Whilst AR may be preceded by allergic eczema, it may also be the first atopic condition recognised⁶⁰. Allergic hypersensitivity may be limited to the nasal cavity and not affect the whole body⁶¹.

In paediatric cases, AR involves at least two of the following: nasal itching and blockage, sneezing and running nose. A careful history covering symptomatology, length of illness, frequency of recurrence and exacerbating features is vital for diagnosis and classification. Being exposed to the allergen plays a key role in provoking symptoms, which may begin after minutes and persist for several hours. The later phases are characterised by nasal congestion, hyper-responsivity, postnasal rhinorrhoea and reduced ability to smell⁶². Child cases of AR may have symptomatic manifestations affecting the lungs, pharynx and ears in addition to the nasal manifestations. Children's life quality may also decrease through being unable to sleep and the resulting tiredness may reduce their ability to concentrate and hamper scholastic performance⁶³.

Having AR puts patients at significant risk of becoming asthmatic at any stage in their life⁶⁴. Additionally, it has been shown that paediatric AR has an association with impaired pulmonary function, increases in exhalation of nitric oxide and hyper-responsivity of the bronchi⁶⁵.

Yet, despite being the most frequently encountered chronic pathological condition in children, management and diagnosis are often deficient and attention to the condition missing. Suboptimal management of AR means life quality declines, the risk of asthma increases, and pre-existing asthma worsens. To manage AR well, it needs to be diagnosed accurately, allergenic exposure should be avoided and medication provided in the form of saline spray, antihistamines that are sedation-free, steroidal therapy to the nose or systemically, and

leukotriene antagonists⁶³. Treating AR well improves asthmatic control, and better-controlled asthma improves AR, too^{66,67}. Giving steroids topically in the nose rarely causes problems and the procedure may be undertaken without undue risk from the age of two onwards⁶⁸⁻⁷¹. The safety profile⁷² of newer corticosteroids (i.e., fluticasone propionate⁷³, mometasone furoate⁷⁴) is more favourable *vis-à-vis* growth velocity restriction than older agents (beclomethasone and budesonide)⁷⁵. Non-sedating antihistamines are a beneficial adjunct to nasal steroids in terms of symptom management^{52,76-80}. First generation antihistamines have sedating effects^{55,60}, however, in appropriate cases they can also be considered for treatment. The sole treatment capable of disease modification is allergen-specific immunotherapy, which offers the possibility of prolonged remission^{55,81-83}, whilst also reducing the chance that asthma may subsequently develop⁸⁴.

Atopic dermatitis in adolescents

Some 10-20% of children with allergic dermatitis (AD) remain symptomatic during adolescence⁸⁵⁻⁸⁷. AD incidence in adolescence varies from 5-10% in the majority of European states to 15-20% in the UK or South America and up to 5% in Asia, according to ISAAC Phase III published results⁸⁷. The typical trigger in such cases is inhaled allergen (particularly pollen from grass or birch) or food allergy (FA) to plants. Rarely, it may be FA to animal protein²⁴. Common associations/comorbidities of AD are other atopic conditions which are reported as FAs, asthma and AR/rhinoconjunctivitis⁸⁸.

AD occurs more frequently in males up to the age of two⁸⁹⁻⁹¹, but thereafter girls in puberty and women are most affected⁹². There are exacerbations in the condition pre-menstrually and during menstruation, hinting at a link between endocrine factors and the pathogenesis of AD^{93,94}.

AD characteristically begins before age two, with the site affected being linked to age. In infants, AD lesions are for the most part found on the head and facial regions (especially chin, malar and frontal aspects) and the extensor surfaces of the limbs. The lesions are exudative. Older children, by contrast, mostly have lesions on the flexor surfaces of the arms and legs, dorsal surface of the hands, back of the feet and the knee and elbow creases. Skin dryness and lichenification with pronounced pruritus are typical presenting features in AD, whilst fissuring of the lips, which are dry and chapped, also frequently occurs. The periocular areas may develop hyperpigmentation from persistent inflammation. Clinically, the disorder presents as a series of exacerbations followed by remission. Remission mainly coincides with sum-

mer, whilst flare-ups are common in autumn and winter⁹⁵. For an adolescent case, the usual presenting signs are eczema affecting the eyelids, palmar and plantar surfaces⁹⁶. Other potential sites for lesions to be seen are the frontal and perioral facial regions, flexor surfaces of the lower limb, dorsum of the hand, superior aspect of the chest and the shoulder girdle²⁴.

Newly published research on 367 US adolescents with allergic conditions showed that anxiety and atopic respiratory disorders were significantly associated, but the relationship did not hold for AD. However, the adolescents involved did have a reduced life quality resulting from pruritus and sleep impairment⁹⁷.

Food allergy in adolescents

There are four principal allergens that account for the majority of cases of food allergy (FA) in young children^{98,99}: milk from cows, chicken eggs, wheat and soya. A rise in cases of groundnut allergy has newly been reported, especially in the UK and US, where rates are estimated at 0.5% and 0.6%^{100,101}. Madsen, however, states that groundnuts are not a principal allergen in cases of FA in large parts of Europe, except for in France and the UK¹⁰².

The rate of perceived FA by patients (20-30%) greatly exceeds that formally diagnosed by clinicians (2-8%)¹⁰³⁻¹⁰⁹. Sloan and Powers¹⁰⁹ researched how the American general public views food-related issues, concluding that experiencing FA symptomatology was reported by one in three households and measures to modify the diet to avoid the “allergen” had been put in place. Given that such modification may result in a dietary restriction not authorised by a clinician, malnourishment of a severe degree is possible in apparent cases of FA¹¹⁰⁻¹¹⁶. Cases of FA in children and teenagers show features of a “Western Lifestyle” between 2%¹⁰⁷ and 4.6%^{103,108} of the time.

In situations where a patient with FA ingests the relevant allergen, the release of IgE may trigger a systemic response that poses a threat to life¹¹⁷⁻¹²⁰. Hence, any such allergens should be scrupulously eliminated from the dietary intake. Such individuals will also need to be given detailed information about where the allergen may be included in foods to stop inadvertent ingestion^{103,121}.

According to Roehr et al., children and adolescents perceive apparent symptoms of FA more frequently than people do in general¹⁰³. Despite this raised incidence, most symptoms were mild and principally attributable to pollen-associated FA. Non-allergic sensitivity to food was less frequent in this group. Patients who already have a diagnosis of allergy may be more at risk of severe FA responses

mediated through IgE, so if FA is suspected, exhaustive investigation will be needed¹⁰⁴.

White and colleagues¹²² found that FA was the leading trigger for anaphylaxis, regardless of severity, timing or geographical location. In 21.8% of cases of anaphylaxis, the victim had no prior awareness of what caused the event.

CONCLUSIONS

AR represents a significant risk factor for becoming asthmatic, whether in childhood, adolescence or adulthood. AD and FA are also frequent conditions during adolescence. Pollen-associated FA constitutes an important part of FA. Furthermore, FA may be the leading trigger for anaphylaxis. Common associations/comorbidities of AD reported are other atopic conditions such as FAs, asthma and AR/rhinoconjunctivitis.

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