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Food adverse reactions in patients over 14 years of age suffering from atopic eczema

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Adverse reactions to food represent one of the most common complaints in the general population and particularly in childhood. Only few population-based data exist on the association of food adverse reactions and atopic eczema (AE). The objective of this study was an assessment of anamnestic data in patients with AE obtained in questionnaires and statistical evaluation of the relations among individual parameters monitored, which include the occurrence of adverse food reactions, the onset of AE, occurrence of asthma bronchiale (AB), occurrence of seasonal or perennial rhinoconjunctivitis (RC). Our findings have demonstrated that the onset of AE before 5 years of age is statistically significantly related to a greater incidence of adverse food reactions at an adult age and to more frequent flare-ups of AE caused by food. Our study demonstrates that there is a significant association between the severity of AE and the incidence of perennial RC, AB, and the worsening of AE in relation to food.

Keywords: atopic eczema; adverse food reactions; asthma bronchiale; rhinoconjunctivitis; allergy; foods

Introduction

Atopic eczema (AE) is one of the earliest manifestations of atopy with the highest incidence during the first three months of life (Bonifazi & Meneghini, 1989) and constitutes together with allergic rhinitis and asthma bronchiale (AB), the triad of atopic diseases. The presence of atopic disorders implies an increased risk of food allergy, which represents only a small percentage of all adverse reactions to foods. Up to 80% of children with AE will eventually develop allergic asthma later in childhood, particularly those who are already sensitised to foods allergens, egg in particular (Arshad et al., 2001; Guillet & Guillet, 1992). It is important to recognise that there are a number of other immunologic and non-immunologic reactions that can produce symptoms after exposure to foods or food additives. These reactions include conditions that are considered to be examples of food intolerance and conditions that are considered to be neither food allergy nor food intolerance.

The aim of our study was the evaluation of the history of patients with AE on the basis of questionnaire, where the patients especially describe the possible occurrence

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of adverse food reactions. These questionnaires were important for the retaining of patients for a future examination of food allergy. The role of food allergens remains controversial and underestimated by older children and adult patients suffering from AE, few studies exist concerning the food allergy in this group of patients. In studies with limited numbers of selected patients, it was shown that severe eczema may be worsened by foods in adulthood as well (Worm et al., 2006), this is particularly true for pollen-associated foods. The role of food allergens for eczematous reactions in AE with a diagnostic algorithm for the elucidation of such late reactions to foods was given in the position paper of the EAACI and GA2LEN (Werfel et al., 2007).

There are also an insufficient number of reports focusing on severity and the duration of AE as risk factors for other manifestations of atopy. The objective of this study was also the statistical evaluation of the relations among individual parameters monitored, which include the occurrence of adverse food reactions, the onset of AE, occurrence of AB, occurrence of seasonal or perennial rhinoconjunctivitis (RC).

The individuals included in the study were all the patients suffering from AE as defined the Hanifin-Rajka criteria and they were examined and treated for AE at the Department of Dermatology and Venereology, University Hospital and Medical Faculty of Charles University, Hradec Králové, Czech Republic.

Methods

Study subjects

In the period from January 2005 to June 2007, 225 patients suffering from AE in the age of 14 years and older – 148 women, 77 men, average age 27.9 (standard deviation 11.3, minimum age 14 years, maximum age 70 years) – completed the questionnaires at the Department of Dermatology and Venereology, University Hospital and Medical Faculty of Charles University, Hradec Králové, Czech Republic. All patients were personally asked by the physician during the dermatological examination to complete the questionnaire. The points which were unclear to the patient were explained to them. The answers concerning the possible adverse food reactions reflect the patients history and were not based on the results of examinations (as specific IgE, skin prick tests or challenge tests).

The questionnaire with the patient's answers were collected and processed by the dermatologist.

Questionnaire

Patients evaluated and answered the following questions:

The occurrence of AB – the patients answered if the positive AB was diagnosed by allergologist.

The occurrence of perennial RC – the patients answered if they suffered from tearing or rhinitis during the whole year.

The occurrence of the seasonal RC – the patients answered if they suffered from tearing or rhinitis during some period in the year.

Severity of AE – the patients evaluate the form of AE as mild, moderate or severe.

The occurrence of food adverse reactions – the patients answered if they suffered from immediate or late food adverse reactions including oral allergic syndrome, gastrointestinal problems, from the occurrence of skin problems, and respiratory problems. The most frequent food allergens are mentioned in the questionnaire and patients answered if they have a suspicion of food adverse reactions, potentially they should have mentioned other foods with suspicion of food adverse reactions.

The worsening of AE in relation with food – the patients answered if they observed the worsening of AE in relation to some foods. Foods in this question were not specified.

The first manifestation of AE – the patients answered when the onset of AE was recorded: up to age of 4 years, from 5 to 17 years of age, from 18 years or over.

The duration of eczematous lesions in the last year of monitoring – the patients answered if they suffered from eczematous lesions constantly during the previous year or only occasionally in a specific period of the year.

Statistical analysis

Pairs of these categories were entered in contingency tables and the Chi-square test for independence of these variables was performed with the level of significance set to 5%. The results were processed in the Department of Medical Biophysics, Medical Faculty of Charles University, Hradec Králové.

Results

The results of the occurrence of follow-up categories and their statistical analysis are summarised in four tables.

Table 1 indicates the occurrence of the parameters observed in patients with AE – the occurrence of AB, perennial RC, seasonal RC, the occurrence of different forms of severity of AE, the occurrence of food adverse effects, the worsening of AE in

Table 1. Occurrence of monitored parameters in per cents in patients with AE (from 225 patients).

Parameter	Percentage (%)
AB	28.4
Perennial RC	37.8
Seasonal RC	48.9
Mild form of AE	29.3
Moderate form of AE	50.2
Severe form of AE	20.4
Adverse food reactions	67.1
Worsening of AE in connection with food	60.0
Onset of AE before 5 years of age	66.2
Onset of AE from 5 years to the end of 17 years of age	17.3
Onset of AE after 18 years of age	16.4
Persistent eczematous lesion in last year	53.7
Occasionally eczematous lesions in last year	46.2

connection with food, the beginning of AE before 5 years of age, the first symptoms of AE, the occurrence of permanent lesions and occasional lesions during the last year of monitoring.

Table 2 shows a comparison of the onset of AE with the mentioned parameters. We proved that the onset of AE is positively related to the occurrence of adverse food reactions and to worsening of AE in connection to food. On the other hand, no relation has been found between the onset of AE and the incidence of AB, perennial RC, and seasonal RC.

Table 3 demonstrates (in per cent) the incidence of perennial RC; the mild, moderate and severe form of AE; as well as the occurrence of food adverse reactions; the worsening of AE in connection to food; and the duration of AE in patients suffering from AB, as compared to patients without AB. We confirmed in our study that all these parameters are related significantly to the occurrence of AB.

Table 4 demonstrates the occurrence of the parameters monitored in connection with different forms of severity of AE. There is a statistically significant association between the severity of AE and the incidence of perennial RC, AB, the worsening of AE in connection with food and with the occurrence of eczematous lesions in last year of monitoring – this association is expressed bold in this table. We did not confirm the relation between the severity of AE and the occurrence of adverse food reactions and the seasonal RC.

The relation between the occurrence of adverse food reactions and the incidence of both perennial RC and AB were evaluated and corroborated. In patients with AB, more frequent adverse food reactions were recorded (in 79%), as compared to patients without AB (in 62%), p -value is 0.01. In patients suffering from perennial RC, the occurrence of adverse food reactions was determined in 78% of patients, while in patients without perennial RC, such reactions occurred only in 60% of cases; the difference is also statistically significant (p -value 0.01). But in both groups of patients (in patients with and without AB and in patients with and without perennial RC, respectively), the occurrence of food adverse reactions is high.

On the other hand, we did not confirm that there is a statistically significant relation between the occurrence of seasonal RC and the occurrence of adverse food reactions and worsening of AE in connection to food in patients with AE in our study.

Table 2. The onset of AE and the occurrence of follow-up parameters in the examined patients (significant relation is expressed bold).

Onset of AE	Adverse food reactions	Worsening of AE in connection with food	Occurrence of AB	Occurrence of perennial RC	Occurrence of seasonal RC
Before 5 years of age (%)	72	69	30	39	50
From 5 years to the end of 17 years of age (%)	66	56	23	43	58
After 18 years of age (%)	45	27	24	24	32
p -Value	0.0088	0.00000	0.524	0.163	0.053

Note: Pairs of these categories were entered in contingency tables and the Chi-square test for independence of these variables was performed with the level of significance set to 5%.

Table 3. Occurrence of parameters in patients with AB (AB+) and in patients without AB (AB-) – all data show statistically significant relation to AB (bold).

Parameter	AB+ (%)	AB – (asthma no.%)	p-Value
All the year RC	66	27	0.0000
Mild form of AE	14	35	0.003
Moderate form of AE	56	47	0.003
Severe form of AE	29	16	0.003
Food adverbs reactions	79	62	0.01
Worsening of AE in connection to food	73	54	0.009
Persistent eczematous lesions last year	67	48	0.01

Note: Pairs of these categories were entered in contingency tables and the Chi-square test for independence of these variables was performed with the level of significance set to 5%.

The relation between perennial RC and persistent eczematous lesions last year was evaluated. Patients with perennial RC suffer in 34% with occasionally eczematous lesions and in 41% with persistent eczematous lesions; patients without perennial RC suffer in 66% with occasionally eczematous lesions and in 58% with persistent eczematous lesions. Statistically significant correlation between incidence of perennial RC and persistent eczematous lesions is not confirmed.

Discussion

The study was based on the evaluation of the data of history given by patients in completing the questionnaires. Though the patients evaluate their course of AE subjectively, their answers could demonstrate their quality of life, especially in questions dealing with the occurrence of food adverse reactions and the severity of AE. All patients were monitored on a long-term basis at our department. The questionnaire was discussed personally with every patient and any points unclear to the patients were explained to them.

The questionnaires in this study served for the retaining of patients suffering from AE with suspicion of adverse food reactions for the future detailed examination in the diagnostic work-up of food allergy.

Table 4. Occurrence of monitored parameters in per cents in mild, moderate and severe form of AE (significant relation expressed bold).

Severity of AE	Perennial RC	AB	Worsening of AE with food	Persistent eczematous lesion last year	Adverse food reactions	Seasonal RC
Mild (%)	24	14	44	20	57	38
Moderate (%)	42	32	65	60	69	51
Severe (%)	46	41	69	87	73	59
p-Value	0.02	0.00319	0.005	0.00000	0.129	0.07

Note: Pairs of these categories were entered in contingency tables and the Chi-square test for independence of these variables was performed with the level of significance set to 5%.

In discussion, we compare our results with similar studies dealing with the course of AE, but there is not enough original data to support our conclusions.

Studies from diverse industrialised regions of the world reveal an increasing prevalence of all clinical manifestations of allergic diseases (Schultz-Larsen & Hanifin, 2002). Prevalence of these diseases has increased by two- to three-fold during the past three decades in industrialised countries. It remains much lower in agricultural regions, such as China, Eastern Europe and rural Africa. Moreover, higher prevalences have been recorded in urban regions than in rural regions of developed countries and the disease is more common in higher social class groups (Taylor, Wadsworth, Wadsworth, & Peckham, 1984).

In 45% of children, the onset of AE occurs during the first six months of life; during the first year of life in 60% of children; and before the age of five years in at least 85% of affected individuals (Kay, Gawkrödger, Mortimer, & Jaron, 1994). In those children with the onset before the age of two years, 20% would have persisting manifestations of the disease and an additional 17% will have intermittent symptoms by the age of seven years. According to Yates, Kerr, and Mackie (1983), AE is one of the earliest clinical manifestations of allergic disease with the highest incidence during the first three months of life. In adults with AE, only 16.8% had an onset after adolescence (Williams & Strachan, 1998). The result of our study also shows that 16% of patients recorded the onset of AE after 18 years of age.

AE that develops during the first year of life is a risk mark for later development of AB and is associated with sensitisation to respiratory allergens and wheezing (Bergmann, Edenharter, & Bergmann, 1998). Prospective cohort studies estimate that those patients with infantile AE have a two- to nine-fold increased risk of developing AB (Martinez et al., 1995).

The results of our study have not shown a significant relation of the onset of AE in patients older than 14 years to the occurrences of AB and RC. This could be explained by the fact that the patients with a mild form of AE or without eczematous lesions already but suffering from AB symptoms do not visit a dermatologist; they are checked only by an allergologist. The drawback of our study also may be that patients with AE mentioned only the onset of AE, but not the onset of AB and the RC.

There are an insufficient number of reports focusing on severity and the duration of AE as risk factors for other manifestations of atopy (Ricci et al., 2006). The risk factor of evolving from AE to other allergic manifestation has only been partially investigated: in a study by Ohshima, Yamada, Hiraoka, and Katamura (2002), risk for developing AB was associated with the persistence of AE. Our study showed that the severity of AE, the occurrence of perennial RC and the occurrence of persistent eczematous lesions in last year are significantly related to the occurrence of AB. Our results showed that the severity of AE was significantly related to the occurrence of perennial RC as well. But we did not prove that there is statistically significant association between incidence of perennial RC and persistent eczematous lesions.

The severity of AE seems to be directly correlated with the severity of the asthmatic response. Brinkman et al. (1997) compared bronchial effects of allergen challenge in patients who had concomitant AE and AB with a range of disease severities. Patients with coexisting severe AE and mild AB developed the most pronounced late asthmatic responses after allergen challenge, leading the authors to suggest that disease mechanisms that are activated in AE may predispose patients to airway inflammation. Finally, it has been suggested that the allergen sensitisation that

occurs via the skin in patients with AE also evokes a strong systemic allergic response, characterised by elevations in serum immunoglobulin E (IgE) antibodies, eosinophils, macrophages and T-cells. These biological markers of leukocyte activation have been shown to correlate with the severity of AE and also may play a role in respiratory allergy in genetically predisposed individuals (Beck & Leung, 2000).

According to the study of Ricci et al. (2006), the severity of AE can predict AB onset. The shift from mild to moderate severity of AE nearly doubles the risk of AB onset. The shift from moderate to severe quadruples the risk. Our study proved that the severity of AE is significantly related to the occurrence of AB, although in a different ratio. The claim by Ricci et al. (2006) that the probability of AB increases with the severity of AE was confirmed as well. It has been suggested that the progression of clinical signs of AE, AB and allergic RC follow each other in time and may coincide (Bousquet, Van Cauwenberge, Khaltaev, Aria Workshop Group, & World Health Organization, 2001; Spergel, 2005; Spergel & Paller, 2003). Allergic RC has been found in 75% of patients with AB (Bousquet et al., 2001), 78% of asthmatics have RC (Gustafsson, Sjoberg, & Foucard, 2000). Up to 80% of children with AE will develop allergic airway disease at some point in childhood (Leung, 2000). In 40–50% of children, this allergic airway disease manifests as AB (Leung, 2000). It is frequently observed that some patients “outgrow” their AE as respiratory allergy develops. Nevertheless, it is estimated that 15–30% of patients with AE have coexistent AB (Leung, 2000) – this is in agreement with our study. The co-occurrence or progressive appearance of atopic diseases supports the idea of the march of atopic disease over a lifetime (Ricci et al., 2006). Moreover, nasal and bronchial mucosa share many similarities that may contribute to this comorbidity. Additionally, nasal challenge triggers the release of mediators that cause bronchial constriction in turn (Bousquet et al., 2001). In our study, we have proved that the incidence of perennial RC depends significantly on the occurrence of AB.

Our study describes the occurrence of food adverse reactions in patients with AE. Adverse reactions are generally divided on a basis of the underlying pathophysiologic changes that produced the reaction as food allergy, food intolerance, pharmacologic reactions, food poisoning and toxic reactions. Although adverse reactions to foods are common, food allergy represents only a small percentage of all adverse reactions to foods, only 2–4% of these food adverse reactions can be attributed to reproducible and IgE-mediated food allergy (Roehr et al., 2004; Zuberbier et al., 2004).

According to Sicherer and Sampson (2009), food allergy, defined as an adverse immune response to food proteins, affects as many as 6% of young children and 3–4% of adults in westernised countries and their prevalence appears to be rising. The importance of food allergy in children with AE was confirmed by extensive studies (Sampson, 1988; Sampson & Scanlon, 1989). The role of food allergy remains controversial and underestimated in older children and adult patients suffering from AE (Schultz-Larsen & Hanifin, 2002; Werfel et al., 2007). Our aim in this study is to evaluate the occurrence of food adverse reactions in adult patients suffering from AE and consecutively to examine them in the diagnostic work-up of food allergy in another study.

According to Mattila et al. (2003), food hypersensitivity is commonly suspected, especially among adults with atopic diseases. Symptoms of food hypersensitivity vary from oral allergic syndrome (burning in the mouth after contact with different kinds of fruits, vegetables and nuts) to gastrointestinal, respiratory and systemic reactions,

as was also noticed in our study. But the authors (Mattila et al., 2003) stressed that more data are needed regarding patient groups at risk for food hypersensitivity and symptoms and foods responsible for the reactions. In the study of Mattila, 286 Finnish university students were examined; 87 of them without clinically confirmed atopic disease, the rest suffered with AE and/or other atopic diseases. A thorough clinical examination was performed with a questionnaire specifying adverse events to foods. Food hypersensitivity was reported by 172 subjects (60%); it was most frequent among subjects with AE – among those with current AE in 73% with past AE in 66% and with RC and AB in 63%. Our study shows similar results. Although we confirmed in our study in statistics that in patients with AE and other atopic diseases (AB or perennial RC) more frequent occurrence of food adverse reactions was recorded in comparison with patients without AB or perennial RC, we should emphasise that in all these patients the occurrence of food adverse reactions is high and the 17% difference (respectively, 18%) from practical point of view is not substantial.

In another study of Williams, Burr, and Williams (2004), the questionnaire was used for children (12–14-year olds) suffering from AE to determine the distribution and relative importance of 19 potential exacerbating and relieving factors. In this paper, food seems to be the less important exacerbating factors for AE; this was considered as a surprise finding by the authors. But the patients suffering from AE in our study are older – the average age is almost 28 years.

On the other hand, we did not prove in statistics that in patients with persistent eczematous lesions more frequent food adverse reactions were described. Nevertheless, our present study has already demonstrated that food adverse reactions and food-induced flare-ups of AE are significantly associated with the onset of AE before the fifth year of age. Adverse food reactions and flare-ups of AE due to food are also significantly related to the incidence of AB and to perennial RC. Flare-ups of AE due to food are also significantly related to the severe form of AE.

The study of Gustafsson et al. (2000) recorded a higher incidence of food allergy in patients with severe form of AE, but no significance between the early onset of AE and the occurrence of food allergy. Our study demonstrates that the onset of AE before five years of age is significantly related to the occurrence of food adverse reactions and to flare-ups of AE in adolescents and adults. According to the study of Ricci et al. (2006), egg sensitisation doubles the risk of the onset of AB and allergic RC.

The results of our study documented the possible role of foods not only with respect to flare-ups of AE, but also as important triggering factors in the occurrence of AB and RC. Similar findings were described in the study of Dunlop, Reichrtova, Palcovicova, and Ciznar (2006).

Conclusion

Food adverse reactions are described in 67% of patients suffering from AE over 14 years of age and 60% of patients have suspicion of food as a triggering factor for the worsening of AE. The patients with severe form of AE describe flare-ups in response to food statistically more frequently than the patients with mild or moderate form.

The study shows that the onset of AE before the fifth year of age is significantly positively related to the occurrence of food adverse reactions and to the occurrence of flare-ups of AE in response to food in adolescents and adults. But there is not

enough original data to support our conclusion, more data are needed regarding patient groups at risk for food hypersensitivity and foods responsible for the reactions.

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