

Evaluation of food allergy to wheat, cow milk, egg, soy and peanuts in patients suffering from atopic dermatitis

J. Čelakovská^{a*}, K. Ettlerová^b, K. Ettler^a, J. Vaněčková^a and J. Bukač^c

^aDepartment of Dermatology and Venereology, Faculty Hospital and Medical Faculty of Charles University, Hradec Králové, Czech Republic; ^bDepartment of Allergy and Clinical Immunology, Outpatient Clinic, Hradec Králové, Czech Republic; ^cDepartment of Medical Biophysics, Medical Faculty of Charles University, Hradec Králové, Czech Republic

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Few large studies concerning the importance of food allergy in adolescents and adult patients with atopic dermatitis exist. The evaluation of food allergy to egg white and yolk, peanuts, soy, cow milk and wheat in patients suffering from atopic dermatitis. Two hundred forty patients (70 men, 170 women) were examined. Complete dermatological and allergological examination was performed in all patients, including specific IgE, skin prick test and atopy patch test. The challenge test was performed according to the results of examinations with suspected foods. The food allergy to peanuts was confirmed in 20% of patients, to egg in 6%, to soy in 3.3%, to wheat in 2.5% and to milk in 0.8% – altogether in 65 patients (27.5%). The positive results in examinations without clinical symptoms of food allergy were recorded in another 78 patients (32.5%). The diagnostic work-up should comprise not only the laboratory methods, but also the diagnostic hypoallergenic diet and the challenge test.

Keywords: atopic dermatitis; food allergy; specific IgE; atopy patch tests; challenge tests

Introduction

Atopic dermatitis is a chronic intermittent inflammatory skin disease that may be in some cases associated with food allergies, especially in early childhood. In about 90% of the cases, the food allergy is caused by cow milk, hen's egg, soy, wheat, fish, peanuts or tree nuts (Suh, 2010). Regarding the course of food allergy, it is well known that about 50–80% of children with allergy to milk or hen's egg develop tolerance until school age (Kjaer, Eller, Andersen, Høst, & Bindslev-Jensen, 2009). Allergies to seafood, peanuts and nuts are more likely to persist (Lack, 2008). Food allergy may be the result of a failure to develop tolerance or the loss of preexisting tolerance. Preliminary results indicate that defects in the epidermal and the gut barrier function may facilitate sensitisation to allergens through epicutaneous and gastrointestinal exposure. Among adults, allergies to cow milk, wheat and hen's egg are rare, although exact data are not available. Aside from allergies persisting since childhood, in Northern and Central Europe, allergies to birch pollen-related foods (hazelnut, carrot, celery, apples) are more common. However, birch pollen-associated food allergy also may be clinically relevant in

*Corresponding author. Email: jarmila.celakovska@seznam.cz

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younger children, especially in children with severe atopic dermatitis and a high sensitisation level to birch pollen (Breuer et al., 2004). According to Sicherer, both atopic dermatitis and food allergy are, in majority of individuals, transitory conditions that improve with increasing age (Sicherer & Sampson, 1999).

In patients with suspected food allergy, which is thought to be aggravating atopic dermatitis, it is therefore important that any food avoidance measures suggested are based on a detailed history and supportive evidence from objective allergy tests as the measurement of specific IgE (serum-specific IgE level – sIgE; skin prick tests – SPT, atopy patch tests [APTs] and challenge tests: open exposure test – OET, double-blind, placebo-controlled food challenge test – DBPCFC). DBPCFC remains the golden standard in diagnosis of food allergy (Niggemann, Reibel, Roehr, & Wahn, 2001).

Aim of the study is to evaluate the occurrence and the clinical symptoms of allergy to foods such as egg white and yolk, peanuts, soy, cow milk and wheat and especially to evaluate if these foods can deteriorate the course of atopic dermatitis.

Methods

Patients over 14 years of age with atopic dermatitis (as defined by the criteria of Hanifin & Rajka, 1980) were examined at the Department of Dermatology at the Faculty Hospital in Hradec Králové (Czech Republic) from January 2005 to April 2012.

Inclusion criteria for the study include

- age 14 years and over
- moderate and severe form of atopic dermatitis – evaluated with SCORAD index (Scoring Index of Atopic Dermatitis) – affected skin area, intensity criteria and subjective parameters are evaluated with this index, (Kunz et al., 1997)
- mild form of atopic dermatitis only with a suspicion to food allergy to various food allergens or with a suspicion to adverse food reactions

Exclusion criteria include long-term therapy with cyklosporin or systemic corticoids, pregnancy and breastfeeding.

Examinations

Complete dermatological and allergological examinations were performed in all included patients.

The detailed history about possible food allergy was taken in all included patients. The SPT, the APT and the measurement of sIgE were performed. Egg white and yolk, peanuts, soy, cow milk and wheat were the examined foods. The examinations were performed after the discontinuation of antihistamines and topical steroids for at least five days and systemic steroids and UV therapy for at least two months.

The diagnostic hypoallergenic diet was recommended to introduce before the OET in all patients with positive results at least in one of the diagnostic methods to examine foods (sIgE and/or SPT and/or APT and/or history – only late reaction with suspicion of worsening of atopic dermatitis). The challenge test with egg white and yolk, soy, cow milk and wheat were performed in patients with positive results at these examinations. OET was not done in patients with early allergic reaction (as oral allergy syndrome, breathlessness, anaphylaxis). Because of anaphylactic reaction, danger peanuts were not examined in the challenge test.

SPT and specific IgE

Commercial food extract Soluprick (ALK Abelló, Denmark) was used for SPT with cow milk. Commercial food extract Alyostal (Stallergens, France) was used for SPT with egg white and yolk, peanuts, soy and wheat.

SPT were placed on the volar side of the forearm according to the extent of atopic dermatitis. SPT were carried out by a standardised method using the lancet with a 1-mm tip. The result was read after 15 minutes and was assessed by comparison with the wheal induced with histamine (10 mg/ml) and a negative control. A wheal with a diameter greater than 3 mm in comparison with a negative control was scored as positive one.

The serum level of the specific IgE to egg white and yolk, peanuts, soy, cow milk and wheat has been measured with the method of fluorescent enzyme immunoassay (FEIA) (Pharmacia CAP system, Uppsala, Sweden). The level of specific IgE higher than 0.35 U/ml was assessed as positive.

APTs

APTs were performed on non-lesional, non-abraded, untreated skin of the back during a remission. A technique similar to conventional patch tests has been used by performing atopy patch testing – CURATEST F strip (Lohmann & Rauscher International GmbH, Germany) with a 12-mm cup size. The APTs with native egg white and yolk, peanuts, soy, cow milk and wheat were applied. The occlusion time of APTs was 48 hours, the first results were evaluated 30 minutes after removal of the tests and the second results were analysed 72 hours after the application of the tests.

Grading of positive APTs reactions was similar to the criteria used in conventional contact allergy patch testing with the modifications of the European task Force on Atopic Dermatitis Consensus Meetings (Darsow et al., 2004). Only reactions from + (erythema, infiltration) onwards were designated positive.

The diagnostic hypoallergenic diet and the OET

We recommended these foods in the period of four weeks: gluten-free foods, potatoes, rice, meat – beef, pork, vegetable and fruits only after thermal modification, but parsley, celery and seasoning were not allowed. The patients were allowed to drink only drinking water, mineral water or black tea. OET was performed after this diet in intervals without symptoms or during a consistent period with regard to atopic dermatitis (not in pollen season in patients with pollen allergy).

In general, the OET was recommended to perform with three doses of examined foods given during two days. One dose of examined food is given in incremental dosages in 10-minute intervals during one hour. The OET was performed with 200 ml of fresh milk in one dose, with wheat flour in the form of pasta (one dose = 200 g of pasta prepared from wheat flour and water), with well-cooked egg and with soy flakes (one dose = 100 g soy flakes). The food challenge results were scored as positive if one or more of the following objective and subjective clinical reactions were noted: itching, rash, urticaria, angioedema, vomiting, wheezing, abdominal pain, diarrhoea, pruritus or worsening of atopic dermatitis. Early reactions were defined as clinical symptoms within two hours after the ingestion of food and late symptoms if occurring after more than two hours. In this case, the physician or the patient recorded worsening of the atopic dermatitis or some other reactions during the OET, the patient continued in the elimination of suspected food and the severity of atopic

dermatitis was evaluated every three month during one year. If the OET was negative, the patient introduced this food in the diet regimen. The severity of atopic dermatitis was evaluated during the ingestion of food over a period of three months during one year. If there was a suspicion to food allergy to more than one food, the next OET was performed in two to three weeks after the first exposure test.

Determination of allergy and sensitisation to examined food

- (1) Patients with the positive result in OET (early and/or late reactions) with examined food and with the positive result at least at one of the diagnostic method (sIgE, APT and SPT) were considered as the patients with food allergy. The early and the late reactions in OET were evaluated.
- (2) Patients with the early reaction after the ingestion of examined food in their history from their childhood and with the positive result at least at one of the diagnostic method (sIgE, APT and SPT). The OET was not performed in these patients because of anaphylactic reaction danger.
- (3) Sensitisation to food was confirmed in patients with positive results in sIgE and/or SPT and/or APT and negative results in OET and in history.

Statistical analysis

The evaluation, if there is some association in patients suffering from atopic dermatitis and food allergy (or sensitisation) to the gender. 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%.

Results

Patients

Altogether 240 persons suffering from atopic dermatitis were included in the study: 70 men and 170 women entered the study with 26.4 (s.d. 9.1 years), min. 14 and max. 63 years; with the median SCORAD 31.3 points, s.d. 13.1 (max. 79.5 points, min. 12.5 points) at the beginning of the study.

Clinical outcomes of challenges

All 240 patients were subjected to SPTs, APTs, sIgE to wheat, peanuts, cow milk, soy and egg white and yolk.

Positive results in personal history and/or sIgE and/or SPT and/or APT to milk was recorded in 38 patients from 240; from these 38 patients, the food allergy to milk was confirmed in two patients – in one patient (0.4%) as worsening of atopic dermatitis in OET and as oral allergy syndrome in another patient (0.4%).

Positive results in personal history and/or sIgE and/or SPT and/or APT to wheat was recorded in 41 patients; from these 41 patients, the food allergy was confirmed in six patients (2.5%) in OET as worsening of atopic dermatitis.

Positive results in personal history and/or sIgE and/or SPT and/or APT to peanuts were recorded in 83 patients. From these 83 patients, the food allergy with the symptoms

of early allergic reaction as oral allergy syndrome was recorded in 48 patients (20%); the OET was not performed because of anaphylactic reaction danger.

Positive results in personal history and/or sIgE and/or SPT and/or APT to soy was recorded in 60 patients; from these 60 patients, the food allergy was confirmed altogether in 8 patients (3.3%) – as early allergic reaction in four patients (1.6%) and as worsening of atopic dermatitis in another four patients (1.6%) in OET.

Positive results in personal history and/or sIgE and/or SPT and/or APT to egg was recorded in 60 patients; from these 60 patients, the food allergy was confirmed altogether in 14 patients (5.6%). Worsening of atopic dermatitis was recorded in nine patients (4%) in the OET; the early allergic reaction in the history – as breathlessness and oral allergy syndrome – was recorded in another five patients (2%).

Altogether the suspicion to food allergy to wheat, egg, cow milk, soy and peanuts was found in 143 patients from 240 (60%), but after evaluation of the challenge test and early reactions in the history, the food allergy was confirmed in 65 patients (27%). From these 65 patients, 11 patients suffer from allergy to two or more of examined foods and 54 suffer from allergy to one of examined food. Table 1 shows the survey of results of food allergy in group of 240 patients suffering from atopic dermatitis. Table 2 shows the number of patients with food allergy (the results of examination to milk, wheat, peanut, soy and egg white and yolk in OET in comparison to the results of examinations in SPT, sIgE and APT and history). Table 3 shows the recorded symptoms of food allergy.

The worsening of atopic dermatitis after ingestion of examined food was confirmed altogether in 17 patients from 240 (7%); elimination of these foods was recommended to these patients. The severity of atopic dermatitis in these patients was evaluated for times in a year during one to three years. The skin finding improved in 13 patients (5.4%).

From the number of 143 patients with positive results in examinations in sIgE and/or SPT and/or APT, no clinical reactions were found in 78 patients (32%) in the challenge test. The sensitisation only to one of the examined foods was recorded in 36 from these 78 patients; the sensitisation to two or more of examined foods is recorded in 42 patients. The sequence of foods with recorded sensitisation is as follows: soy in 52 patients (22%),

Table 1. The survey of results of all examinations to food allergy in group of 240 patients suffering from atopic dermatitis.

Number of patients – 240		
Negative results in sIgE and/or SPT and/or APT and/or history 97 (40%) patients	Positive results in sIgE and/or SPT and/or APT and/or history – suspicion to food allergy 143 (60%) patients	
	Allergy confirmed – 65 patients (27.5%), 54 patients allergic to one food and 11 patients allergic to two and more foods	Sensitisation – 78 patients (32.5%), 36 patients sensitised to one food and 42 patients sensitised to more than one food
	Peanuts 48 patients (20%)	Soy 52 patients (22%)
	Egg 14 (6%)	Egg 46 (19%)
	Soy 8 (3%)	Peanuts 35 (15%)
	Wheat 6 (2.5%)	Wheat 29 (12%)
	Milk 2 (0.8%)	Milk 26 (11%)

Table 2. The number of positive results in examinations to milk, wheat, peanut, soy and egg white and yolk in SPT, sIgE and APT and history in comparison to the results of open exposure test and confirmed food allergy.

Suspicion to food allergy from 240 patients – number of positive results in examinations									
Food	No. of patients	SPT	IgE	APT	Personal history	Early reaction in history	Positive result in OET	Food allergy confirmed	Sensitisation (no clinical symptoms of food allergy)
Milk	38	7	18	3	14	1	1	2 (0.8%)	26 (11%)
Wheat	41	17	7	13	6	0	6	6 (2.5%)	29 (12%)
Peanut	83	44	25	11	48	48	n.d.	48 (20%)	35 (15%)
Soy	60	42	14	14	4	4	4	8 (3.3%)	52 (22%)
Egg white	49	26	26	8	12	5	9	14 (6%)	35 (15%)
Egg yolk	60	17	36	12	10				46 (19%)
Total number of patients	143 (60%)							65 (27%)	78 (32%)

Note: SPT – skin prick test, number of patients with positive results.

sIgE – specific IgE, number of patients with positive results.

APT – atopy patch test, number of patients with positive results.

Suspected food allergy – number of patients with positive results in SPT, sIgE, APT and history to examined foods; some of the patients are suspected to have the food allergy to more than one of examined food.

n.d. – not done.

Table 3. Symptoms of food allergy.

Food	Symptoms of food allergy and number of patients from 240					
	Confirmed food allergy	Oral allergy syndrome	Pruritus	Worsening of atopic dermatitis	GIT symptoms	Anaphylactic reaction, breathlessness
Milk	2 (0.8%)	1	1	1 (0.4%)	0	0
Wheat	6 (2.5%)	0	6	6 (2.5%)	0	0
Peanut	48 (20%)	38	7		7	2
Soy	8 (3%)	4	4	4 (1.5%)	4	0
Egg	14 (6%)	4	9	9 (4%)	0	1
The total number of patients	65 (27%)	45 (19%)	23 (9.5%)	17 (7%)	11 (4%)	3 (1%)

Note: From 65 patients with confirmed food allergy, 11 patients suffer from allergy to two and more foods, 54 patients suffer from allergy to one of examined food.

egg in 46 patients (19%), peanuts in 35 patients (15%), wheat in 29 patients (12%) and milk in 26 patients (11%).

Results of statistical analysis

The number of male and female patients in the sample is not the same and we consider relative frequencies of occurrences of allergy in male (31.7%) and female (18.9%) patients. To see the difference is significant, we arrange the data in a contingency table (gender by allergy). We may reject the hypothesis of independence of the two classifications, p -value = 0.042.

Discussion

The higher prevalence of food allergy is recorded in children with atopic disorders; about 35% of children with moderate to severe atopic dermatitis have IgE-mediated food allergy and about 6–8% of asthmatic children have food-induced wheezing (Novembre, De Martino, & Vierucci, 1988). But 80% of them outgrow their food allergy. In adult patients with atopic dermatitis, studies investigating the co-prevalence of atopic dermatitis and food allergy are still scarce and exact data are not available (Heratizadeh, Wichmann, & Werfel, 2011; Werfel & Breuer, 2004). The results of a population-based study in Germany involving 1739 unselected patients who had completed questionnaires confirmed that food allergy in adult atopic dermatitis patients is rare (Worm et al., 2006).

The main strengths of our study lie in the evaluation of food allergy in large group of patients suffering from atopic dermatitis. The diagnostic procedures indicated to confirm the diagnosis of food allergy, in particular late-type reactions, remain time-consuming because food challenges need to be performed. Studies frequently focus on the assessment of sensitisation via IgE to food allergens rather than on the results of oral food challenges, which are still recommended as the diagnostic ‘gold standard’. According to our results, food allergy to basic foods as wheat, egg, soy, cow milk and peanuts may play an important role in the worsening of atopic dermatitis (acting as a triggering-exacerbating factor) only in a minority of adolescents and adult patients. Moreover, other triggering factors may cause exacerbation of the atopic dermatitis in the patients enrolled in the study. Majority of patients with positive results in sIgE, SPT or APT are only sensitised to these foods without clinical reactions.

For comparison of our results there are no studies dealing with the same question in adolescents and adults patients with atopic dermatitis. In children, some authors correlated allergen-specific serum IgE levels with challenge outcomes (Perry, Matsui, Kay Conover-Walker, & Wood, 2004; Sampson, & Ho, 1997). Benhamou (Benhamou, Zamora, & Eigenmann, 2008) found that egg-specific IgE levels increased significantly in concordance with the severity of allergic reactions. Decision points for specific IgE levels were not established for isolated eczematous reactions yet. Generally, three different clinical patterns are described after ingesting food (Breuer et al., 2004): (1) immediate-type symptoms such as erythema, angioedema, urticaria, but no eczema, bronchial, gastrointestinal or cardiovascular symptoms of anaphylaxis, which appear within minutes after ingesting the relevant food; (2) isolated, eczematous, late-type reactions, which normally appear as flare-ups of typical eczematous lesions occurring within hours to two days after ingestion and (3) combined reaction pattern of non-eczematous, immediate-type reactions and eczematous, late-type reactions.

The sequence of recorded symptoms of food allergy at our study is oral allergy syndrome in 41 patients (17%), pruritus in 23 patients (9.5%), worsening of atopic dermatitis in 17 patients (7%), gastrointestinal problems as abdominal pain and cramps in 11 patients (4.5%) and anaphylactic reaction after egg and peanuts in six patients (2.5%).

In 17 patients from 240 (7%) the worsening of atopic dermatitis after ingestion of examined food was confirmed. All these patients were recommended to eliminate these foods. The severity of atopic dermatitis in patients with positive results in OET was evaluated after elimination of these foods every three months during one to three years. The skin finding improved in 13 patients (5.4%). These patients also suffer from exacerbations of atopic dermatitis, but it is the consequence of other triggering factors, as they describe (stress, inhalant allergens and pollen-associated foods). These patients eliminate these foods from their meal, and during the mild breaking of the diet regimen they can observe after the ingestion of egg, soy, wheat and milk the reactions on the skin, such as the pruritus, erythema and new eczematous lesions. The elimination of these foods did not influence the severity of atopic dermatitis in patients suffering from early reactions in OET and as well did not influence the severity of atopic dermatitis in another four patients with late reactions. These four patients suffer from moderate form of atopic dermatitis and suffer from allergy to common inhalant allergens. After casual ingestion of foods with confirmed allergic reaction they can observe the new eczematous lesions and pruritus.

Sixteen patients from 240 (6%) mentioned, that they had sometimes suspicion to worsening of atopic dermatitis after ingestion of milk (10 patients) and wheat (6 patients). They recorded sometimes pruritus and new eczematous papules as late reactions (8–10 hours after ingestion of foods). All results of examination to these foods were negative, including OET.

But these patients have been suffering from chronic eczematous lesions, with acute exacerbations caused by other triggering factors as pollen allergy, stress or climatic changes.

The sequence of foods responsible for food allergy at our study with recorded early and/or late allergic reactions is as follows: peanuts in 48 patients (20%), egg in 14 patients (6%), soy in 8 patients (3%), wheat in 6 patients (2.5%) and milk in 2 patients (0.8%). At our study, peanuts are the most common food allergens affecting 20% of our patients and causing in majority of them oral allergy syndrome. Peanut allergy represents an increasing problem in Western countries, involving approximately one in 150 to 200 subjects. The mean age at detection is decreasing and also two to three-year-old children are affected. The at-risk subject is an atopic individual, with heightened risk for those with atopic dermatitis and/or other food allergies. The peanut allergy is long-lived for most, may increase slightly in severity over time, but approximately 20% of young children will develop tolerance (Sicherer, 2002).

Egg is the second most common food allergen at our study causing the worsening of atopic dermatitis in nine patients (4%) and early allergic reactions in five patients (2%). Egg allergy is one of the most common food allergies in infants and young children, affecting 1–2% of young children (Heine, Laske, & Hill, 2006). Recent reports indicate that it is taking longer for children to outgrow their egg allergy, with most developing tolerance in their teenage years rather than in early school-age as previously thought (Savage, Matsui, Skripak, & Wood, 2007).

Soy allergy was recorded in four patients as oral allergy syndrome and in another four patients as worsening of atopic dermatitis. But sensitisation to soy was found in another 22% patients without clinical symptoms after soy ingestion. Allergenicity of soybean proteins has been documented since the 1980s, and allergy to soy has been described to date primarily in young children with atopic dermatitis (Niggemann, Sielaff, Beyer,

Binder, & Wahn, 1999; Sampson & Scanlon, 1989; Sicherer, 2000) affecting approximately 0.4% of children (Savage, Kaeding, Matsui, & Wood, 2010). Most patients with soy allergy are likely to develop soy tolerance by late childhood (Savage et al., 2010). Epidemiologic data on soybean allergy in adults are rare (Besler, Helm, & Ogawa, 2000; Hessing, Bleeke, Tsuji, Ogawa, & Vlooswijk, 1996; Sicherer, 2000). The explanation for high soy sensitisation at our study may be the fact that in Central Europe soy is a clinically relevant birch pollen-related allergenic food as well. Crossreaction is mediated by a Bet v 1 homologous protein, Gly m 4.

Wheat allergy, which usually begins in early childhood, is outgrown by three to five years of age in most cases; in adults, food allergy to ingested wheat seems to be infrequent and especially described as an anaphylactic reaction for the most part induced by exercise (food-dependent, exercise-induced anaphylaxis – FDEIA; Morita, Kunie, & Matsuo, 2007). In some cases, IgE-mediated allergy to wheat may lead to worsening of atopic dermatitis or gastrointestinal symptoms (Pérez-Pimiento et al., 2007; Varjonen, Savolainen, Mattila, & Kalimo, 1994). Studies dealing with wheat allergy in adult patients suffering from atopic dermatitis are rare and the significance of food allergy may be underestimated (Worm et al., 2006). Worsening of atopic dermatitis was recorded in our study after wheat ingestion in six patients (2.5%), no early reaction was recorded and sensitisation to wheat appeared in 12% of patients.

Cow milk allergy affects about 2–3% of children in the first year of life (Host, 2002). In patients with cow milk allergy and atopic dermatitis, resolution occurs in 90% by the age of four years. Non-IgE-mediated cow milk allergy often disappears before the age of one year. The role of food allergy to cow milk remains controversial in adolescents and adult patients suffering from atopic dermatitis; no studies concerning the food allergy to cow milk in this group of patients are available (Skripak, Matsui, Mudd, & Wood, 2007). According to our results, cow milk allergy is rare, affecting only 0.8% of patients; sensitisation is recorded in 11% patients.

In patients with sensitisation to examined foods, the severity of atopic dermatitis and the occurrence of the other allergic reactions were evaluated after the introducing of these suspected foods in the common meal. No reactions were observed in these patients after ingestion of these foods during one year.

Conclusion

Food allergy to wheat, soy, egg, peanut and milk is recorded in 27% of patients suffering from atopic dermatitis, another 32% suffer from sensitisation to these foods. The food allergy as a triggering factor causing the exacerbation of atopic dermatitis is recorded in 7% of patients. The diagnostic work-up should comprise not only the laboratory methods, but also the elimination diet and challenge test.

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