EGG ALLERGY IN ADOLESCENT AND ADULT PATIENT SUFFERING FROM ATOPIC DERMATITIS – ASSOCIATION WITH CONCOMITANT ALLERGIC DISEASES

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Summary: Background: A few reports demonstrate the occurrence of egg allergy in adolescent and adult patients suffering from atopic dermatitis and the association of this allergy to other food and aeroallergens. Aims and Objectives: The aim of this study is to evaluate the occurrence of egg allergy in patients suffering from atopic dermatitis at the age 14 years and older and to evaluate the relationship between egg allergy or egg sensitisation and the sensitisation to dust, mites, feather, and animal dander. Materials and Methods: Complete dermatological and allergological examination was performed. These parameters were examined: food allergy and food sensitisation to egg white and yolk, to mites, animal dander (mixture), feather and dust. The statistical evaluation of the relations among egg allergy, egg sensitisation and sensitisation to mites, animal dander (mixture), feather and dust was performed. Two hundred and eighty eight patients were included in the study (90 men, 198 women, with the average age 25.2). Results and Conclusion: Egg allergy was recorded in 5% and egg sensitisation in 20% of patients; sensitisation to dust is recorded more often in patients with positive results in sIgE for egg white and/or yolk.

Keywords: *Atopic dermatitis; Egg allergy; Food allergy; Specific IgE; Open exposure test*

Introduction

Hen eggs are one of the most common causes of food allergic reactions. Egg white, which is generally considered more allergenic than egg yolk, has four major allergenic proteins namely, ovomucoid, ovalbumin, ovotransferrin and lysozyme which are defined as immunodominant egg white proteins (1). Although ovomucoid comprises only 10% of the total egg white protein, it has been shown to be the dominant allergen (2). The most reported allergen from egg yolk seems to be alpha-livetin; the relationship between asthma and rhinoconjunctivitis due to bird feather sensitization and egg allergy has been described as a bird-egg syndrome related to the cross-reactive IgE antibody able to bind the egg yolk livetin and bird feather allergens (3, 4). Egg allergy is one of the most frequent food allergies in children below the age of three years; adult-onset of egg allergy has rarely been mentioned in the literature. The presence of atopic dermatitis is a significant risk factor for this allergy (5) and children with egg allergy are at an increased risk of other allergic diseases especially asthma (odds ratio 5.0) and peanut/nut allergy (6). In a recent meta-analysis the prevalence of egg allergy was estimated to be between 0.5 and 2.5% (7) and the prevalence in the adult population at 0.1% (7). It has been observed from previous reports that egg allergy in adults generally begins in childhood or early adulthood with severe systemic allergic symptoms (8, 9, 10). Egg allergy is generally considered to have a good prognosis, but recent reports indicate that it is taking longer for children to outgrow their egg allergy, with most developing tolerance in their teenage years rather that in early school-age as previously thought (11). The most common symptoms of egg allergy are IgE-mediated erythema, urticaria and eczematous rash occurring in 90% of the children (12). Furthermore, gastrointestinal symptoms, abdominal pain and vomiting (mostly in conjunction with other immediate-type symptoms) occur in 40–50% of cases following egg ingestion. In addition, egg is one of the most common food allergens in allergic eosinophilic esophagitis and allergic eosinophilic gastroenteritis (13).

Diagnosis of food allergy is based on personal history, measurement of specific IgE (serum specific IgE level – sIgE, skin prick tests – SPT), atopy patch tests (APT), challenge test (open exposure test – OET, double-blind, placebo-controlled food challenge) (14). There are no studies dealing with the occurrence of egg allergy in adolescents and adults suffering from atopic dermatitis and evaluating the relationship to other types of allergy.

The aim of this study is to evaluate the occurrence of egg allergy in patients suffering from atopic dermatitis at the age 14 years and older and to evaluate the relationship between egg allergy (egg sensitisation) and the sensitisation to dust, mites, feather, and animal dander. Our other aim is the characteristic of patients with egg allergy and the evaluation, if there are some patients suffering from bird – egg syndrome.

Method

In the period from January 2005 to March 2014, 288 patients suffering from atopic dermatitis at the age 14 years and older were examined. The diagnosis of atopic dermatitis was made with the Hanifin-Rajka criteria (15). Complete dermatological and allergological examination was performed. These parameters were examined: food allergy and food sensitisation to egg white and yolk and sensitisation to mites, animal dander (mixture), feather and dust.

Evaluation of parameters monitored

The diagnosis of food allergy to egg (to yolk and white) was made according to the results in specific IgE (sIgE), in skin prick tests (SPT), in atopy patch test (APT) and in the open exposure tests (16). Open exposure test took two days with three doses of examined food in the interval of 12 hours also, but one dose was divided into incremental dosages given during 80 minutes. The well-cooked egg was applied at 20-minute intervals with incremental dosages – 50 mg, 500 mg, 5 g, 50 g, and 100 g. The first day the patient consumed the dose of egg at 8:00 a.m., the reaction was observed and in the case of no response the second dose of food was consumed at 6:00 p.m. If no response resulted, the last dose challenge was administered the next day at 8:00 a.m. The patient recorded the reaction also during the 48 hours after the last dose. The skin was scored by the SCORAD system before the elimination diet, during the elimination diet and before OET and then 24 and 48 hours after OET.

The food challenge results were scored as positive if one or more of the following objective and subjective clinical reactions were noted: urticaria, angioedema, vomiting, wheezing, abdominal pain, diarrhea, oral allergic syndrome, pruritus, erythema, rashes or worsening of atopic eczema (evaluated with SCORAD). Early reactions were defined as clinical symptoms within 2 hours after the ingestion of the dose in OET and late symptoms if occurring after more than 2 hours.

Patients with the positive result in the open exposure test (early and/or late reactions) with egg and with the positive result at least in one of the diagnostic method (sIgE, APT, SPT) to egg white and/or yolk were considered as the patients with egg allergy. Patients with the early reaction after the ingestion of egg repeatedly in their history from their childhood were considered as patients with egg allergy also; the open exposure test was not performed in these patients because of anaphylactic reaction danger (16).

Sensitisation to egg white and yolk was confirmed in patients with the positive results in sIgE and/or SPT and/or APT, but with the negative results in the open exposure test to these food allergens.

Sensitisation to dust, mites, animal dander (mixture), feather (mixture)

It was determined according to the specific IgE level and the skin prick test (SPT) results for these allergens. Commercial extracts Alyostal (Stallergens, France) was used for SPT. The serum level of the sIgE has been measured with the method of CAP (system FEIA – Pharmacia Diagnostics, Uppsala, Sweden). The level of specific IgE higher than 0.35 U/ml was assessed as positive. Mite, cockroach and animal allergens are major components of house dust.

Statistical analysis

It was evaluated, whether there is any relationship in atopic dermatitis patients at the age 14 years and older, who suffer from egg allergy or egg sensitisation to the occurrence of sensitisation to mites (Dermatophagoides pharinae, pteronnyssinus), animal dander, feather, and dust (Mite, cockroach and animal allergens are major components of house dust).

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

Results

Altogether 288 patients suffering from atopic dermatitis were included in the study: 90 men and 198 women entered the study with the average age 25.2 years (s.d. 9.2 years), min.14 max. 63 years. The results of the occurrence of follow-up categories and their statistical analysis are summarized in three tables.

Table No. 1. The occurrence of the tested parameters observed in patients with atopic dermatitis is recorded in this table 1. From 288 patients (100%), egg allergy was recorded in 15 patients (5%), egg sensitisation in 58 patients (20%), sensitisation to mites in 175 patients (61%), to dust in 63 patients (22%), to animal dander in 128 patients (44%), to feather in 38 patients (13%).

Table No. 2. The relationship between the occurrence of food allergy to egg and the occurrence of followed parameters is shown in Table No 2. From tested parameters, the significant relationship was found only between patients suffering from egg sensitisation and dust sensitisation. No

other significant relationship was found between patients with egg allergy or egg sensitisation and sensitisation to animal dander, mites and feather.

Table No. 3. Characteristic of patients with egg allergy is recorded in this table.

The egg allergy was confirmed in 15 patients (in three men and 12 women). In the open exposure test, the egg allergy was confirmed in 11 patients and the symptoms of early and late skin reactions were recorded in these patients. The gastrointestinal symptoms such as abdominal pain and diarrhoea were recorded in patients No. 3, 8, 11 as well. Oral allergy syndrome and asthma were recorded in four patients as early reaction after egg ingestion from early childhood – in these patients with positive history about egg allergy the open exposure test was not performed because of danger of anaphylactic reaction. Positive results in specific IgE (sIgE) for both egg white and egg yolk was recorded in nine patients, only positive finding of IgE for egg yolk was found in four patients and for egg white in one patient. No specific IgE for egg white and egg yolk was found in one patient with the symptom of oral allergy syndrome from early childhood after egg ingestion. The level of sIgE for egg white was recorded from 0.42 to 22.9 U/ml, for egg yolk from 0.6 to 22.25 U/ml.

Tab. 1: The occurrence of the tested parameters observed in patients with atopic dermatitis.

Parameters	Number of patients (from 288 – 100%)
Egg allergy	15 (5%)
Egg sensitisation	58 (20%)
Sensitisation to mites	175 (61%)

Parameters	Number of patients (from 288 – 100%)
Sensitisation to animal dander	128 (44%)
Sensitisation to feather	38 (13%)
Sensitisation to dust	63 (22%)

Tab. 2: Number of patients with egg allergy (+) and without egg allergy (−) and the occurrence of tested parameters in these patients. The correlation is shown extra bold.

	Number of patients with or without sensitisation to the tested parameters							
Egg allergy/sensitisation	mites +	mites −	dander +	dander −	feather +	feather −	dust +	dust −
Egg Allergy +	9	6	3	12	3	12	6	9
Egg Allergy −	166	107	125	148	35	238	57	216
Total No. of patients	175	113	128	160	38	250	63	225
p-value	0.950377		0.05035		0.4237		0.08114	
Egg Sensitisation +	40	18	27	31	7	51	19	39
Egg Sensitisation −	135	95	101	129	31	199	44	186
Total number of patients	175	113	128	160	38	250	63	225
p-value	0.15229		0.717796		0.776863		**0.0248**	

Tab. 3: Characteristics of patients suffering from egg allergy.

No. of patient, birth, sex	The level of sIgE – egg white, egg yolk (U/ml)	OET	Food allergy	Inhallant allergy	Rhinitis	AB
1, 1986, F	–	OAS	nuts	mites, grass	+	+
2, 1973, F	egg white 22.92 egg yolk 9.14	+	nuts	animal dander, mites, feather	+	+
3, 1977, F	egg white 4.43 egg yolk 2.18	+	nuts, chicken meat	grass, pollen	+	+
4, 1990, F	egg white 2.44 egg yolk 2.34	+	nuts	animal dander, mites, feather	+	+
5, 1991, M	egg white – egg yolk 7.28	+	nuts	mites, grass	+	+

6, 1990, F	egg white – egg yolk 8.10	+	chicken meat, nuts	grass	+	–
7, 1969, F	egg white 4,19 egg yolk 4.36	OAS	soy, wheat flour	pollen, mites	+	–
8, 1991, F	egg white 9.38 egg yolk 1.58	OAS	fish	mites	+	+
9, 1986, F	egg white – egg yolk 7.79	+	nuts, fish	pollen, mites, animal dander	+	+
10, 1974, F	egg white 3,29 egg yolk –	OAS	fish, tomatoes	feather, mites	+	+
11, 1953, F	egg white 7.29 egg yolk 4.7	+	fish, nuts	feather, mites animal dander	+	+
12, 1985, F	egg white 0.89 egg yolk 0.60	+	fish, nuts, milk	pollen, birch	+	+
13, 1981, F	egg white 0. 42 egg yolk 22.25	+	soy, fish	–	–	–
14, 1962, M	egg yolk 0.5	+	–	mites, animal dander, pollen	+	+
15, 1989, M	egg yolk 1.69 egg white 1.16	+	–	pollen, peanuts	+	–

Explanation: AB – asthma bronchiale, OET – open exposure test, OAS – oral allergy syndrome
+ positive result, – negative result

Discussion

The occurrence of egg allergy in atopic dermatitis patients and the relationship to the sensitisation to common inhalant allergens was evaluated in 288 patients examined in this study. Double-blind, placebo-controlled food challenge (DBPCFC) remains the golden standard in diagnosis of food allergy and although the unequivocal diagnosis of egg allergy requires a double-blind, placebo-controlled food challenge (17, 18), open food challenges, which are less resource-intensive, are generally considered sufficient in clinical practice.

The statistically significant relationship was recorded between patients suffering from egg and dust sensitisation. No relationship was confirmed between patients suffering from egg allergy or egg sensitisation and the sensitisation to mites, animal dander and feather. The egg allergy was confirmed in 15 patients, in five of them the allergy started in early childhood, in ten patients this allergy appeared later and at these patients, the symptoms were recorded mainly as later skin reaction with the worsening of atopic dermatitis and some gastrointestinal problems (such as abdominal pain and diarrhoea). According to the literature, egg allergy in adults is likely to be severe and long-lasting and is due either to persistent childhood egg allergy or to true adult-onset egg allergy, such as occupational, for example, in workers from the baking industry who develop sensitization by inhalation (10), part of the bird-egg syndrome with an allergy to egg yolk (19) or egg-white allergy after eggs have been tolerated for years (20).

Strong association between sensitisation to egg during infancy and sensitisation to inhalant allergens later in childhood has been observed by several groups (21). According to our results, the relationship was confirmed in patients suffering from egg sensitisation only to dust sensitisation, but not to the mites, animal dander and feather sensitisation. According to one study, food allergens from milk, peanut, egg, and fish were frequently detected in dust samples from mattresses of Norwegian adolescents (22). Another study has described peanut protein in dust collected from mattresses of infants and their parents (23) and egg, milk, and fish allergens have previously been described in dust samples collected from floors (24).

Although the occurrence of asthma bronchiale and rhinitis was recorded in majority of patients with egg allergy, the significant relationship between egg allergy and the occurrence of asthma bronchiale, rhinitis and pollen allergy was not confirmed at our previous study (25). The recorded symptoms of egg allergy at our study are oral allergy, worsening of atopic dermatitis and gastrointestinal symptoms. Oral allergy syndrome was recorded in four patients, in another 11 patients the early and/or late reaction on the skin was recorded as pruritus, maculopapulous rash and worsening of eczematic lesions. The late, non-IgE-mediated reaction to egg may play a role in a small number of individuals with atopic dermatitis and is characterised by

a clinical flare of the atopic dermatitis typically between 4 and 48 h following ingestion and is postulated to be T cell mediated (26). In a small study, Lever *et al.* reported an improvement in atopic dermatitis following egg elimination, particularly in those subjects with pre-existing IgE sensitisation to egg (27). Positive results in sIgE (specific sIgE, skin prick tests) for egg white and/or yolk without clinical symptoms after egg ingestion were recorded in 58 patients (20%). At our study, no relationship was found between patients with allergy to egg and sensitisation to bird feather. But from 15 patients suffering from egg allergy, there are three patients with positive sIgE to yolk (patients No. 2, 4, and 11) and with positive results in sIgE and /or skin prick tests to bird feather and as well to animal dander. All these patients suffer from asthma bronchiale and rhnitis and suffer from acute respiratory problems in contact with parrots and animal dander. Another two patients (No. 3 and No. 6) with positive sIgE to yolk suffer from gastrointestinal problems after ingestion of chicken meat. A combination of bird-feather sensitization and egg allergy has been named the bird-egg syndrome. The patients diagnosed as having bird-egg syndrome were usually adult females and they also had sensitization to animal fur. Bird- egg syndrome is characterized by respiratory and gastrointestinal symptoms. Asthma is the main symptom as a consequence of contact with birds and rhinoconjunctivitis may develop. Sensitization to bird proteins precedes development of egg allergy, although sometimes the order of appearance is reversed. Typically, patients develop upper and lower respiratory symptoms on exposure to birds and gastrointestinal symptoms with chicken meat or lightly cooked eggs. The likely allergen is chicken serum albumin Gal d 5 and the egg allergy is due to IgE cross-reactivity with livetin found in egg yolk (4). Egg yolk contains significant quantities of serum proteins, since livetins are derived from the blood of the hen. Williams identified livetin as chicken serum albumin (CSA), a protein of 65–70 kDa (28). Szépfalusi (3) pointed out that CSA is a cross-reactive allergen in the bird-egg syndrome. De Maat-Bleeker et al. first reported the association of hypersensitivity to ingested egg yolk with rhinitis and asthma caused by exposure to a parrot in an older woman (29). By RAST inhibition, Mandallaz et al. demonstrated that livetin, the water-soluble fraction of egg-yolk proteins, was the major cross-reacting antigen found in bird feathers and egg yolk, and they coined the term "bird-egg syndrome" to designate this IgE-mediated association of inhalant and food allergy (30). Although the examination for livetin was not done at our study, the patients with egg allergy, positive sIgE for yolk and clinical symptoms after contact with birds, animal dander or after ingestion of chicken meat can suffer from bird-egg syndrome.

Conclusion

Egg allergy was recorded in 5% and egg sensitisation in 20% of patients suffering from atopic dermatitis; the occurrence of bird-egg syndrome is suspected in five patients (1.7%). Sensitisation to dust is recorded more often in patients with positive results in sIgE for egg white and/or yolk.

References

1. Ibtissam O, Amal, E, Lotfi A. Modulation of egg white protein allergenicity under physical and chemical treatments. Food and Agricultural Immunology 2011; 1: 57–68.
2. Bernhisel-Broadbent J, Dintzis H, Dintzis R, Sampson H. Allergenicity and antigenicity of chicken egg ovomucoid (Gal d III) compared with ovalbumin (Gal d I) in children with egg allergy and in mice. J Allergy Clin Immunol 1994; 93: 1047–1059.
3. Szépfalusi Z, Ebne C, Pandjaitan R et al. Egg yolk α-livetin (chicken serum albumin) is a cross-reactive allergen in the bird-egg syndrome. J Allergy Clin Immunol 1994; 93: 932–942.
4. Quirce S, Maranon F, Umpierrez A, De Las H, Fernandez-Caldas E, Sastre J. Chicken serum albumin (Gal d 5*) is a partially heat-labile inhalant and food allergen implicated in the bird-egg syndrome. Allergy 2001; 56 (8): 754–62.
5. Monti G, Muratore M, Peltran A, Bonfante G, Silvestro L, Oggero R, Mussa G. High incidence of adverse reactions to egg challenge on first known exposure in young atopic dermatitis children: predictive value of skin prick test and radioallergosorbent test to egg proteins. Clin Exp Allergy 2002; 32: 1515–9.
6. Tariq S, Matthews S, Hakim E, Arshad S. Egg allergy in infancy predicts respiratory allergic disease by 4 years of age. Pediatr Allergy Immunol 2000; 11:162–7.
7. Osterballe M, Hansen T, Mortz C, Host A, Bindlev-Jensen C. The prevalence of food hypersensitivity in an unselected population of children and adults. Pediatr Allergy Immunol 2005; 16(7): 567–73.
8. Nogaard A, Bindslev-Jensen, C. Egg and milk allergy in adults. Allergy 1992; 47(5): 503–9.
9. Asero R, Mistrello G, Roncarolo D. Unusual egg allergy in an adult. Allergy 1995; 54: 1328–36.
10. Escudero C, Quirce S, Fernandez-Nieto M, Miguel J, Cuesta J, Sastre J. Egg white proteins as inhalant allergens associated with baker's asthma. Allergy 2003; 58: 616–20.
11. Savage J, Matsui E, Skripak J, Wood R. The natural history of egg allergy. J Allergy Clin Immunol 2007; 120: 1413–1417.
12. Boyano Martinez T, Garcia C, Diaz-Pena J et al. Validity of specific IgE antibodies in children with egg allergy. Clin Exp Allergy 2001; 31: 1464–1469.
13. Sampson H, Sicherer S, Birnbaum A. AGA technical review on the evaluation of food allergy in gastrointestinal disorders. American Gastroenterological Association. Gastroenterol 2001; 120: 1026–1040.
14. Niggemann B, Reibel S, Roehr C, Wahn U. Predictors of positive food challenge outcome in non-IgE-mediated reactions to food in children with atopic dermatitis. J Allergy Clin Immunol 2001; 108 (6): 1053–8.
15. Hanifin J, Rajka G. Diagnostic features of atopic dermatitis. Acta Derm Venereol 1980; 92: 44–47.
16. Čelakovská J, Ettlerová K, Vaněčková J, Ettler K. Egg allergy in patients over 14 years of age suffering from atopic eczema. Int Journal of Dermatol, 2011; 50: 811–818.
17. Niggemann B, Reibel S, Roehr C, Wahn U. Predictors of positive food challenge outcome in non-IgE-mediated reactions to food in children with atopic dermatitis. J Allergy Clin Immunol 2001; 108: 1053–8.
18. Bock S, Sampson H, Atkins F et al. Double-blind, placebo-controlled food challenge (DBPCFC) as an office procedure: a manual. J Allergy Clin Immunol 1988; 82: 986–997.
19. Anibarro B, Martin E, Martinez A, Pascual M, Ojeda Casas J. Egg protein sensitization in patients with bird feather allergy. Allergy 1991; 46: 614–8.
20. Unsel M, Sin A, Ardeniz O et al. New onset egg allergy in an adult. J Investig Allergol Clin Immunol 2007; 17: 55–8.
21. Wang J, Visness C, Sampson H. Food allergen sensitization in inner-city children with asthma. J Allergy Clin Immunol 2005; 115: 1076–1080.
22. Bertelsen R, Faeste C, Granum B et al. Food allergens in mattress dust in Norwegian homes – a potentially important source of allergen exposure. Clin Exp Allergy 2014; 44(1): 142–9.
23. Brough H, Santos A, Makinson K et al. Peanut protein in household dust is related to household peanut consumption and is biologically active. J Allergy Clin Immunol 2013; 132: 630–8.
24. Witteman A, van Leeuwen J, van der Zee J, Aalberse R. Food allergens in house dust. Int Arch Allergy Immunol 1995; 107: 566–8.
25. Čelakovská J, Bukač J. Food allergy in patients suffering from atopic dermatitis – association with concomitant allergic dieases. Food and Agricultural Immunology 2014, 10.1080/09540105.2014.914470.
26. Breuer K, Heratizadeh A, Wulf A et al. Late eczematous reactions to food in children with atopic dermatitis. Clin. Exp. Allergy 2004; 34: 817–824.

27. Lever R, MacDonald C, Waugh P, Aitchison, T. Randomised controlled trial of advice on an egg exclusion diet in young children with atopic eczema and sensitivity to eggs. Pediatr Allergy Immunol 1988; 9: 13–19.
28. Williams J. Serum proteins and the livetins in hen's egg yolk. Biochem J 1962; 83: 346–355.
29. De Maat-Bleeker F, Van Dijk A, Berrens L. Allergy to egg yolk possibly induced by sensitization to bird serum antigens. Ann Allergy 1982; 55: 245–248.
30. Mandallaz M, De Weck A, Dahinden C. Bird-egg syndrome. Cross-reactivity between bird antigens and egg-yolk livetins in IgE-mediated hypersensitivity. Int Arch Allergy Appl Immunol 1988; 87: 143–150.

Received: 16/12/2014
Accepted in revised form: 25/03/2015

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