Altogether 332 patients of AD 14 year or older were included in the study.

Hypersensitivity reaction, inhalant allergy

Key Words: Allergic rhinitis, allergy to peanuts, asthma bronchiale, atopic dermatitis, food hypersensitivity reaction, inhalant allergy

Abstract

Background: In adult patients suffering from atopic dermatitis (AD), studies investigating the co-prevalence of AD and food allergy are still scarce, and exact data are not available. Aims and Objectives: To evaluate the occurrence of food allergy to peanuts in significant relation to food hypersensitivity, inhalant allergy and to asthma bronchial and rhinitis. Materials and Methods: Altogether 332 patients of AD 14 year or older were included in the study. The complete dermatological and allergological examinations were performed in all included patients (including examination of specific immunoglobulin E, skin prick test to different food and inhalant allergens, anamnestic data about food reactions, evaluation of allergic rhinitis, and allergic asthma bronchiale). We evaluated whether there was some relation between the food allergy to peanuts and followed parameters. Pairs of these categories were entered in the contingency tables, and the Chi-square test for the relationship of these variables was performed with the level of significance set to 5%. Results: Altogether 332 persons suffering from AD were included in the study of which 120 were male and 212 were female; the average age was 27.2 year. The significant relation between the allergy to peanuts and the occurrence of food hypersensitivity (FH) reactions to tomatoes, kiwi, apples, oranges, carrot and to the sensitization to grass, trees, mites, and the occurrence of rhinitis was found. Conclusion: The significant relation between the allergy to peanuts and the occurrence of FH reactions and the sensitization to inhalant allergens and rhinitis was found. The future studies may show if the decrease in food allergy to peanuts can lead to the decrease of the occurrence of other FH reactions and sensitization to inhalant allergens and rhinitis in AD patients.

Introduction

In adult patients suffering from atopic dermatitis (AD), studies investigating the co-prevalence of AD and food allergy are still scarce and exact data are not available.[1-3]

In this study we evaluate the occurrence of food allergy to peanuts in AD patients older than 14 years of age and the relation of this allergy to the occurrence of asthma bronchiale, rhinitis, the occurrence of food hypersensitivity reactions (FH reactions), and sensitization to inhalant allergens. AD usually starts in infancy and affects two of ten children and it is also highly prevalent in adults. It was originally regarded as a childhood disorder mediated by an imbalance toward a T-helper-2 response and exaggerated immunoglobulin E (IgE) responses to allergens, it is now recognized as a lifelong disposition with variable clinical manifestations and expressivity in which defects of the epidermal barrier are central.[4] The progression of atopic disorders from AD in infants to allergic rhinitis and asthma in children is usually described as atopic march.[4,5] AD increases the risk of food allergy, asthma, allergic rhinitis, other...
Recent data indicate that peanut allergy is on the rise. Peanuts are the seeds of the peanut plant (*Arachis hypogaea*), a member of the legume family (Fabaceae). The peanut is botanically related to peas and beans but not to tree nuts. Peanuts are very rich in nutrients and are one of the basic crops of India, China, the USA, and West Africa. Peanuts contain 44%-56% of oil and 22%-30% of protein. All known peanut allergen classes were determined to consist of 85% of the total protein content of peanut, while Ara h 1, Ara h 2, and Ara h 3 together accounted for 75%. Peanut allergy has been well described and widely reported with population prevalence estimates between 1% and 6%. The latest findings showed that early sustained consumption of peanut products was associated with a substantial and significant decrease in the development of peanut allergy in high-risk infants. Conversely, peanut avoidance was associated with a greater frequency of clinical peanut allergy than peanut consumption was. It raises questions about the usefulness of deliberate avoidance of peanuts as a strategy to prevent allergy.

The term food allergy is used to describe the clinical symptoms that are mediated by the immune system; number of IgE-mediated, cellular-mediated, and mixed IgE-mediated and cell-mediated food hypersensitivity disorders have been described. However, different kinds of food reactions may appear. The term FH reactions represent an umbrella term for food allergy and for nonallergic food hypersensitivity (= food intolerance). Food intolerance is a nonallergic hypersensitivity to food that does not include the immune system even though the symptoms are similar to those of IgE-mediated allergic reactions. An impaired histamine degradation based on reduced diamine oxidase activity and the resulting histamine excess may cause numerous symptoms mimicking an allergic reaction.

The occurrence of food allergy to peanuts was evaluated in our several studies. We recorded, that the food allergy to peanuts can play an important role in atopic march in patients suffering from AD. Patients suffering from these reactions to peanuts eliminate these foods usually from early childhood because of early or late food reactions and there is a question if the elimination of these foods can influence the onset of other food or inhalant reactions. The aim of this study is to show if the occurrence of food allergy to peanuts is in significant relation to the occurrence of other food and inhalant allergy (such as grass, trees, mites, animal dander, bird feather, dust, tomatoes, kiwi, apple, spices, oranges, citruses, celery, strawberries, carrot, and capsicum), as well to asthma bronchiale, and allergic rhinitis.

**Materials and Methods**

During the period 2008–2017, 332 patients suffering from AD at the age of 14 year or older were examined. All these patients were examined at the Department of Dermatology, Faculty Hospital Hradec Králové, Charles University in Prague, Czech Republic. The diagnosis of AD was made with the Hanifin and Rajka criteria. Exclusion criteria were long-term therapy with cyclosporin or systemic corticoids, pregnancy or breastfeeding. Patients with AD having other systemic diseases were excluded from the studies as well. Complete dermatological and allergological examination were performed in patients included in the study (including examination of specific IgE (sIgE), skin prick test (SPT) to different food and inhalant allergens, anamnestic data about food intolerance, evaluation of allergic rhinitis, allergic asthma bronchiale), the detailed description was recorded on previous studies. The severity of AD was evaluated with a SCORAD system. The diagnosis of food allergy to peanuts was made according to the results in sIgE, SPTs, atopy patch test (APT), and according to the anamnestic data about the food reactions to peanuts. Due to an anaphylactic reaction, peanuts were not examined in the challenge test. The study was approved by the Ethics committee of Faculty Hospital Hradec Králové, Charles University in Prague, Czech Republic. There was no conflict of interest. CONSORT statement and STROBE statement guidelines were followed.

The diagnosis of food hypersensitivity reactions to other food allergens (tomatoes, kiwi, apple, spices, oranges, citruses, celery, strawberries, carrot, and capsicum) was made according to the patient’s history. The patients answered whether they had suffered from immediate or late food reactions (oral allergy syndrome (OAS), gastrointestinal problems, the occurrence of skin problems, and respiratory problems). The most frequent food allergens were mentioned, and patients answered whether they had suffered from some reactions to these foods, potentially they should have mentioned other foods with recorded reactions. The answers concerning possible food reactions reflected the patient’s history and were not based on the results of examinations such as specific IgE, SPTs, or challenge tests. The results of examinations with the patient’s answers were collected and processed by the dermatologist.

Sensitization to mites, animal danders, dusts, bird feathers, mixture of grasses, and mixture of trees was
confirmed according to the specific IgE levels and SPTs. Commercial extracts Alyostal (Stallergens, France) was used for SPT. The serum level of the sIgE was 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.

The diagnosis of asthma bronchiale was made according to the results in spirometry at allergological outpatients department and according to the data about wheezing. Asthma was diagnosed with at least three separate episodes of wheezing, each at least 3 days in duration during the past year.

The evaluation of allergic rhinitis (seasonal or perennial) was made according to the anamnestic data such as recurrent nasal symptoms/rhinitis (recurrent nasal discharge or blockage with attacks of sneezing and itchy eyes).

Statistical analysis
We evaluated whether there was some relation between the food allergy to peanuts and followed parameters (FH reactions to tomatoes, kiwi, apple, spices, oranges, citrususes, celery, strawberries, carrot, capsicum; the occurrence of asthma bronchiale, rhinitis, sensitization to mites, animal dander, dust, bird feather, mixture of grass, and mixture of trees). Pairs of these categories were entered in the contingency tables, and the Chi-square test for the relationship of these variables was performed with the level of significance set to 5%.

To see in which direction the dependence was, we used the coefficient of concordance (CC). If the CC was positive, the dependence was direct. If the CC be negative, the dependence was indirect.

We used the Excel program and macros to enter the data. We also used the NCSS package for calculations.

Results
Altogether 332 persons suffering from AD of which 120 men and 212 women were included in the study with the average age 27.2 (standard deviation [SD] 9.1) years, minimum 14 and maximum 63 years; with the median SCORAD 30.5 points, SD 12.4 (minimum 12.5 points, maximum 79.5 points) at the beginning of the study.

Allergy to peanuts
All 332 patients were subjected to SPTs, APTs, and sIgE to peanuts. Due to anaphylactic reaction, peanuts were not examined in the challenge test. The diagnosis of food allergy to peanuts was made according to the positive results in sIgE and/or SPT and/or in APT and in positive anamnestic data about food allergy to peanuts. The allergy to peanuts was confirmed in 92 patients (27%). The recorded symptoms were as follows: the OAS in 70 patients (21%), gastrointestinal problems in 14 patients (4%), and pruritus of the skin in 8 patients (2%).

The occurrence of food hypersensitivity reactions
The FH reactions after the ingestion of tomatoes are described in 65 patients (19.6%), kiwi in 62 patients (18.7%), apples in 55 patients (16.6%), spices in 64 patients (19.3%), tangerines in 59 patients (17.8%), oranges in 52 patients (15.7%), capsicum in 35 patients (10.6%), fish in 35 patients (10.6%), celery in 36 patients (10.9%), carrots in 20 patients (60.2%), and to strawberries in 10 patients (3%). More than one kind of reactions were described in some patients (for example pruritus and OAS).

The sensitization to inhalant allergens
The sensitization to mites was confirmed in 203 patients (61.1%), to animal dander in 158 patients (47.6%), to bird feather in 47 patients (14.2%), and to dust in 82 patients (24.7%). The sensitization to mixtures of trees was confirmed in 167 patients (50.3%), and to a mixture of grasses in 225 patients (67.8%).

The occurrence of asthma bronchiale and allergic rhinitis
The diagnosis of asthma bronchiale was recorded in 146 patients (44%) and the diagnosis of rhinitis in 255 patients (76.8%).

The evaluation of the relation between the allergy to peanuts and the occurrence of followed parameters
We recorded the significant relation between the allergy to peanuts and the occurrence of FH reactions to tomatoes (P=0.031), to kiwi (P=0.006), to apple (P=0.010), to oranges (P=0.026), to carrot (P=0.005), [Table 1]. The significant relations were recorded in the occurrence of rhinitis (P=0.001), the sensitization to mites (P=0.003) and sensitization to mixtures of trees (P=0.002) and mixture of grasses (P<0.000), [Table 2].

Discussion
According to our results, the significant relation between the allergy to peanuts and the occurrence of FH reactions to tomatoes, kiwi, apples, oranges, carrot, to the sensitization to grass, trees, mites, and rhinitis was found. The explanation of this relation may be in the fact that the majority of nut allergens are seed storage proteins. Other nut allergens are profilins and pathogenesis-related protein homologs considered to be panallergens because of their widespread distribution in plants.[27] The presence of specific IgE antibodies to several kinds of nuts is a common clinical finding, but the clinical relevance of this cross-reactivity is
usually limited. The increasing prevalence of allergy to peanuts, coupled with the knowledge that allergic reactions to these foods have the potential to be severe or fatal and that accidental exposures are common, makes developing effective treatments to alter the natural history of peanut and tree nut allergies even more crucial for those who will not outgrow them.\[27,28\]

According to the latest results, the early introduction of peanuts significantly decreased the frequency of the development of peanut allergy among children at high risk for this allergy and modulated immune responses to peanuts.\[12\] Among infants with high-risk of atopic disease, sustained peanut consumption beginning in the first 11 months of life, as compared to peanut avoidance, resulted in a significantly smaller proportion of children with peanut allergy at the age of 60 months. This intervention was safe, tolerated, and highly efficacious. Allergens of peanuts belong to the cupin (Ara h 1, Ara h 3), the prolamin (Ara h 2, Ara h 6, Ara h 7), the profilin (Ara h 5), the Bet v 1 (Ara h 8), the glycosyltransferases GT-C (Ara h 10, Ara h 11, Ara h 12).
h 14, Ara h 15), the scorpion toxin-like knottin (Ara h 12, Ara h 13) superfamilies and nonspecific lipid transfer protein (LTP) (Ara h 9, Ara h 16, Ara h 17). Monosensitization to a single peanut allergen is relatively rare.[29] The reason for the significant relation between the allergy to peanuts and inhalant and food allergens in our study may be the result of the cross-reactivity. Cross-reactivity relies on the presence of conserved antibody-accessible surface structures of peanut proteins and hence, it is observed in general between members of the same protein family. Peanut allergens such as Bet v 1 related Ara h 8, the peanut profilin Ara h 5 and the LTP Ara h 9 are regarded as panallergens. Such allergens are responsible for allergic cross-reactivity across a wide variety of unrelated plants and they are often associated with birch and grass pollinosis or involved in nsLTP-syndrome.[29] According to Allen, peanut or tree nut avoidance during pregnancy is not recommended for nonallergic mothers. Maternal nut consumption does not appear to increase the risk of nut allergy in offsprings and may even be protective. Further research is required to clarify the role of maternal nut consumption during pregnancy or lactation; research should consider potential differential effects of the genetic risk of peanut allergy in children.[30] According to another study, it has been well documented that avoidance of allergenic foods is not preventive of food allergy. There is a strong evidence that early introduction of peanuts is in fact preventive. Emerging evidence from randomized controlled trials suggests that early introduction of allergenic foods, specifically peanuts, is protective against the development of food allergy.[31] Recent findings from interventional studies have prompted a shift in the mind set from avoidance to early introduction of potentially allergenic foods.[32] Consensus statements from various global allergy, pediatric and dermatology societies have been published encouraging the early introduction of peanuts to infants at risk of developing food allergy.[33-36] According to Dhar, the prevalence of AD has increased faster than any changes in gene pool would explain. Inherited factors cannot explain this increase, and there should be exogenous reasons for this. There is much interest in possible trigger factors, in particular the ones that are potentially modifiable. There are epidemiological studies attempting to identify reasons for differences in prevalence but, till date, no definitive causation has been identified. In some cases, specific risk factors have been suggested and include house dust mites, exposure to allergens, infections, breastfeeding, use of antibiotics, and irritants. There are conflicting results for some of these factors (e.g., breast feeding) and difficulty with dealing with confounding factors. This complex work supports our knowledge of AD as a complex process and therefore, the etiology is unlikely to be simple or unidirectional.[37] The future studies may show, if the decrease in food allergy to peanuts can lead to the decrease of the occurrence of other FH reactions and sensitization to inhalant allergens and rhinitis in AD patients.

Conclusion

The occurrence of food allergy to peanuts in AD patients was recorded in 27% of patients. The significant relation between the allergy to peanuts and the occurrence of FH reactions to tomatoes, kiwi, apples, oranges, carrot and to the sensitization to grass, trees, mites and to the occurrence of rhinitis was found.

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Conflicts of interest

There are no conflicts of interest.

What is new?

The occurrence of peanut allergy was significantly correlated with other food allergies in adult atopic dermatitis patients.

References

1. Heratizadeh A, Wichmann K, Werfel T. Food allergy and atopic dermatitis: How are they connected? Curr Allergy Asthma Rep 2011;11:284-91.
2. Scott JF, Hammond MI, Nederos ST. Food avoidance diets for dermatitis. Curr Allergy Asthma Rep 2015;15:60.
3. Worm M, Forschner K, Lee HH, Roehr CC, Edenharter G, Niggemann BH, et al. Frequency of atopic dermatitis and relevance of food allergy in adults in Germany. Acta Derm Venereol 2006;86:119-22.
4. Weidinger S, Novak N. Atopic dermatitis. Lancet 2016;387:1109-22.
5. Dharmage SC, Lowe AJ, Matheson MC, Burgess JA, Allen KJ, Abramson MJ, et al. Atopic dermatitis and the atopic march revisited. Allergy 2014;69:17-27.
6. Rückmann H, van Geel MJ, Knulst AC, Huiskes J, Bruijnzeel-Koomen CA, de Bruin-Weller MS, et al. Food allergen sensitization pattern in adults in relation to severity of atopic dermatitis. Clin Transl Allergy 2014;4:9.
7. Alduraywish SA, Lodge CJ, Campbell B, Allen KJ, Erbas B, Lowe AJ, et al. The march from early life food sensitization to allergic disease: A systematic review and meta-analyses of birth cohort studies. Allergy 2016;71:77-89.
8. Manam S, Tsakok T, Till S, Fehr C. The association between atopic dermatitis and food allergy in adults. Curr Opin Allergy Clin Immunol 2014;14:423-9.
9. Sebei K, Grouna A, Herchi W, Sakouhi F, Boukhchina S. Lipids, proteins, phenolic composition, antioxidant and antibacterial activities of seeds of peanuts (Arachis hypogaea L) cultivated in Tunisia. Biol Res 2013;46:257-63.
10. Grimshaw KE, Bryant T, Oliver EM, Martin J, Maskell J, Kemp T, et al. Incidence and risk factors for food hypersensitivity in UK infants: Results from a birth cohort study. Clin Transl Allergy 2015;6:1.
11. Perkin MR, Logan K, Tseng A, Razi B, Ayis S, Peacock J, et al. Randomized trial of introduction of allergenic foods in breast-fed infants. N Engl J Med 2016;374:1733-43.
12. Du Toit G, Roberts G, Sayre PH, Bahnson HT, Radulovic S,
Santos AF, et al. Randomized trial of peanut consumption in infants at risk for peanut allergy. N Engl J Med 2015;372:803-13.

13. Maloney JM, Rudengren M, Ahlstedt S, Bock SA, Sampson HA. The use of serum-specific IgE measurements for the diagnosis of peanut, tree nut, and seed allergy. J Allergy Clin Immunol 2008;122:145-51.

14. Clark AT, Ewan PW. The development and progression of allergy to multiple nuts at different ages. Pediatr Allergy Immunol 2005;16:507-11.

15. Allen KJ, Hill DJ, Heine RG 4. Food allergy in childhood. Med J Aust 2006;185:394-400.

16. Rona RJ, Keil T, Summers C, Gislason D, Zuidmeer L, Sodergren E, et al. The prevalence of food allergy: A meta-analysis. J Allergy Clin Immunol 2007;120:638-46.

17. Osborne NJ, Koplin JJ, Martin PE, Gurrin LC, Lowe AJ, Matheson MC, et al. Prevalence of challenge-proven IgE-mediated food allergy using population-based sampling and predetermined challenge criteria in infants. J Allergy Clin Immunol 2011;127:668-760.

18. Johansson SG, Hourihane JO, Bousquet J, Bruijnzeel-Koomen C, Dreborg S, Haahltela T, et al. A revised nomenclature for allergy. An EAACI position statement from the EAACI nomenclature task force. Allergy 2001;56:813-24.

19. Maintz L, Novak N. Histamine and histamine intolerance. Am J Clin Nutr 2007;85:1185-96.

20. Celakovska J, Bukac J. Atopic dermatitis in adolescents and adults – The evaluation with other allergic diseases and parameters. Food Agric Immunol 2017;28:933-48.

21. Celakovska J, Bukac J. The severity of atopic dermatitis and analysis of the food hypersensitivity reactions. Food Agric Immunol 2015;26:896-908.

22. Celakovska J, Bukac J. Food hypersensitivity reactions and peripheral blood eosinophilia in patients suffering from atopic dermatitis. Food Agric Immunol 2017;28:35-43.

23. Celakovska J, Bukac J, Ettler K. Food hypersensitivity reactions in atopic dermatitis patients and analysis of concomitant diseases. Food Agric Immunol 2015;26:260-70.

24. Moher D, Hopewell S, Schulz KE, Montori V, Getzschke FJ, et al. CONSORT 2010 explanation and elaboration: Updated guidelines for reporting parallel group randomised trials. BMJ 2010;340:c869.

25. Hanifin J, Rajka G. Diagnostic features of atopic dermatitis. Acta Derm Venereol 1980;92:44-7.

26. Severity scoring of atopic dermatitis: The SCORAD index. Consensus report of the European task force on atopic dermatitis. Dermatology 1993;186:23-31.

27. Crespo JF, James JM, Fernandez-Rodriguez C, Rodriguez J. Food allergy: Nuts and tree nuts. Br J Nutr 2006;96 Suppl 2:S95-102.

28. Fleischer DM. The natural history of peanut and tree nut allergy. Curr Allergy Asthma Rep 2007;7:175-81.

29. Shreffler WG, Beyer K, Chu TH, Burks AW, Sampson HA. Microarray immunoassay: Association of clinical history, in vitro IgE function, and heterogeneity of allergenic peanut epitopes. J Allergy Clin Immunol 2004;113:776-82.

30. Allen KJ, Koplin JJ. High consumption of peanuts or tree nuts by non-allergic mothers around the time of pregnancy reduces the risk of nut allergy in the child. Evid Based Nurs 2015;18:45.

31. Abrams EM, Becker AB. Food introduction and allergy prevention in infants. CMAJ 2015;187:1297-301.

32. Du Toit G, Foong RM, Lack G. Prevention of food allergy – Early dietary interventions. Allergol Int 2016;65:370-7.

33. Fleischer DM, Sicherer S, Greenhawt M, Campbell D, Chan E, Muraro A, et al. Consensus communication on early peanut introduction and prevention of peanut allergy in high-risk infants. Pediatr Dermatol 2016;33:103-6.

34. Fleischer D, Sicherer S, Greenhawt M, Campbell D, Chan E, Muraro A, et al. Consensus communication on early peanut introduction and the prevention of peanut allergy in high-risk infants. Pediatrics 2015;136:103-6.

35. Fleischer DM, Sicherer S, Greenhawt M, Campbell D, Chan E, Muraro A, et al. Consensus communication on early peanut introduction and the prevention of peanut allergy in high-risk infants. J Allergy Clin Immunol 2015;136:258-61.

36. Fleischer DM, Sicherer S, Greenhawt M, Campbell D, Chan E, Muraro A, et al. Consensus communication on early peanut introduction and the prevention of peanut allergy in high-risk infants. World Allergy Organ J 2015;8:27.

37. Dhar S, Srinivas SM. Food allergy in atopic dermatitis. Indian J Dermatol 2016;61:645-8.