COMMON FOOD ALLERGENS IN CHILDREN (A REPORT FROM A REFERRAL CENTER IN TEHRAN UNIVERSITY OF MEDICAL SCIENCES)

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Abstract- The prevalence of food allergy is different in various nations. The identification of the most common food allergens is a priority in any population to provide effective preventive and curative measures. The aim of this study is to determine the most common food allergens in Iranian children. One hundred and ninety children with skin, respiratory or gastrointestinal symptoms, which were thought to be due to food allergy, were studied. Total serum IgE and eosinophil count tests were measured in all patients. Allergy to 25 food allergens was determined according to the patient's history, skin prick tests, radioallergosorbent test (RAST) and open food challenge tests. The most common food allergens were cow's milk, tomato, egg white, egg yolk, beef and almond, in decreasing order of frequency. The order of common food allergens in this study was different from other reports that might be due to the different food habits and/or ethnic diversities.

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Key words: Allergens, child, food, food hypersensitivity, radioallergosorbent test, skin tests

INTRODUCTION

"Food allergy" (FA) as it is called today has been the concern of man for centuries and was noticed by many old physicians. Avecina in the 10th century stated that legumes could cause severe headaches and could also induce an attack in asthmatic patients (1). Referring to a similar issue, Fletcher and Beaumont in the early 17th century said "what is one man's poison, is another's meat and drink"; yet, it was not until the nineteenth century that physicians began to pay serious attention to what was called food idiosyncrasy (2). One of the early reports on the role of foods in asthma appeared in 1840 by Roods and in 1855 there appeared a detailed account of a man whose asthma and constitutional symptoms were caused by ingestion of wheat (2). This remarkable report is one of the earliest observations of what is referred to now as FA (2). It seems, however, that FA was noticed as a problem but the knowledge about the diseases linked with it, its diagnostic tests and hypoallergenic diets are all recent developments in this field.

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FA is usually mediated by IgE antibody directed to specific food proteins, but other immunologic mechanisms can also play a role. The primary target organs for food allergic reactions are skin, the gastrointestinal tract and the respiratory system(3). Food allergic reactions are often confined to one target organ, but allergen specific IgE is believed to bind similarly to mast cells in almost all tissue sites (3,4). Failure in diagnosis or treatment of FA may be the cause of serious disturbances to thrive and development of children (5).

Although accurate data of the prevalence of food hypersensitivity are unavailable, it has been estimated that up to 8% of children less than 3 years of age and 2% of adults experience food induced allergic disorders (6). In USA, 6% of children and 1.5% of adults suffer from FA (7). A cross-sectional epidemiological study of FA in 15 countries showed that 12% of respondents had food allergy/ intolerance (range 4.6% in Spain to 19.1% in Australia). Self reported food allergy/intolerance differed significantly across multiple countries that might be due to cultural differences (8). Population studies have shown that prevalence of food allergy in Netherlands, UK, France and Japan are 0.8- 2.4%(9), 1.4-1.8% (10), 3.2% (11) and 12.6% (12), respectively. The order of common specific allergens varies in different countries, reflecting a possible interaction of genetic factors,

cultural and dietary habits and exposure to new allergenic products early in life (13). For example peanut allergy is very common in UK (14), France (15), Switzerland (16) and North America (17), but very rare in Italy (18), Singapore (19) and Israel (13). So, identification of common food allergens in every country is essential for proper diagnosis and treatment of patients with FA, as well as determination of a suitable hypoallergenic diet. The aim of this study is to identify the most common food allergens in Iranian allergic children.

MATERIALS AND METHODS

Patients

In a six year period, all the patients complaining of cutaneous, respiratory or gastrointestinal disorders (40%, 51.6% and 8.4%, respectively), suspected to be due and to FA, and referring to allergy and immunology department of Children Medical Center, with at least two of the following criteria were studied.

1. A clear history of complaints related to food (3) (maximum one hour after ingestion of the offending food) and not being seasonal (20-22).

2. Having elevated serum IgE, eosinophilia or positive familial history of allergy.

3. Onset of disease in the first year of life (2,21-23).

In all patients, total serum IgE level was measured using ELISA method. The kits were obtained from IFCI CloneSystems Company, Bologna, Italy. Also, blood eosinophils were counted (20).

Hypersensitivity to food allergens was studied using skin prick tests, radioallergosorbent test (RASTs) and open food challenge tests. All patients were controlled clinically 2-3 weeks before and during consumption of hypoallergenic diet (about outbreak of rash, hives, vomiting, diarrhea, cough, asthma or any other complaints).

Skin prick test

All patients (except those with severe eczema) underwent skin prick test (24-26) for twenty-five food allergen extracts (shown in table 1) that were selected according to the following three criteria:

- Necessity in children's diet
- Being conventional in Iranian diet
- Being common food allergens according to other reports.

The allergens were purchased from Dome Holister Stier (Miles, Canada). A positive control test with histamine hydrochloride 1 mg/ml and a negative control test with negative control solution (glycerol 50%) were also included. Those with a wheal diameter of at least 5-7 mm in positive control and no response to negative control underwent skin prick test. Skin tests were done using prick method with disposable blood lancets. The resulting wheal and flare reactions of histamine were read at 10 minutes and of allergens at 20 minutes. The skin test was considered positive if the diameter of the wheal was 3 mm or more (24).

Radioallergosorbent Test (RAST)

One milliliter serum of one hundred patients was kept in -70°c (especially, from patients whose parents didn't permit prick test or from infants or patients with severe eczema) (24,25). Fourteen food allergens (containing milk, egg yolk, egg white, fish, melon, chicken, orange, beef, tomato, almond, soy, rice, corn and wheat) were chosen for RASTs.

Allergen coated disks were purchased from Kabi Pharmacia Diagnostics, Uppsala, Sweden. Tests were done according to the instructions given in the kit and the results were categorized to 0-5+, while positive RAST was defined as specific IgE, 2+ or more (27,28).

Hypoallergenic diet

It was chosen on the basis of hypoallergenic food, the essential foods in children's diet and Iranian conventional food (29,30). The hypoallergenic diet was given to all patients and they were controlled clinically 2 weeks before and during consumption of the diet (about outbreak of rash, hives, vomiting, diarrhea, cough, asthma or any other complaints). Duration of taking the diet was 10-15 days except in patients with atopic dermatitis (28) or gastrointestinal disorders that was 3-4 weeks (21,31).

Open food challenge test

The patients responding to hypoallergenic diet through 2-3 weeks and with collaborative parents (96% of patients) were chosen for open food challenge test (32-34). Although double blind Placebo controlled food challenge (DBPCFC) test is the gold standard for diagnosis of FA (33), in infants and young children whose allergy symptoms are predominantly objective (rash, hives, vomiting, diarrhea or decreased pulmonary function test) (26,31,33), in whom the effect of suggestion is minimal (31) and for screening a large number of foods, open or single blind food challenge test may be

utilized (31,32). Those 25 food items were given fresh and were challenged one by one and on different days. Amount of food given to each patient was determined according to his age, weight and clinical symptoms (35). The offending food was brought by patients to the office and then they were challenged with incremental portions of it. Five dilutions of the food were prepared, which were put in contact with perioral skin, and while patients were fasting the five dilutions were given to them to be ingested one by one at 30 minutes intervals. After ingestion of undiluted food, patients were controlled clinically for 2-12 hours. Repetition of any previous complaints of the patients were determined as positive open food challenge test (21,31,33).

When the skin test and/or RAST was negative and history of reaction to the offending food was doubtful, the suspected food was replaced in diet at home (33,36). Open food challenge test (for 5-25 food subjects according to the patient's age) was done in 100 patients (50%).

Those, who had any history of anaphylaxis, generalized urticaria or severe asthma (19 patients [5.5%]) did not undergo the challenge test (36). During the tests, intensive safety measures were taken (37). Those with a positive challenge test or those with positive skin prick test and/or RAST that were exactly compatible with their history, were considered food allergic. According to the patients' age, final results were categorized into four groups (age≤ 1, 1< age≤ 3, 3< age≤ 6, 6< age≤ 12).

RESULTS

One hundred and ninety children (58.5% boys and 41.5% girls, 3 months to 12 years old) were studied. Skin prick test was performed in 171 patients (all patients except those with severe eczema, negative response to positive control or severe dermographism).

Skin prick test in 53.2%, RAST in 45.8% and challenge test in 88.5% were positive to at least one allergen, without any life-threatening reactions. Of the patients, 97.3% responded to hypoallergenic diet. Among them, 87.2% of the patients with respiratory disease and 66.2% with skin disease were improved. Serum total IgE was less than 100 IU/ml in 43.3% of the patients, 100 -299 IU/ml in 22.6%**,** 300-999 IU/ml in 28.3% and more than 1000 IU/ml in 6.2%. Eosinophil count was 350-999 cell/µl in 45.3% of the patients and more than 1000 cell/µl in 9.4%. Common food allergens in different age groups are shown in table 1.

Table 1. Common food allergens in different age group*

	Age Group				
Allergens	**Age ≤ 1 (n= 24)**	**1< age≤ 3 (n= 39)**	**3< age≤ 6 (n= 39)**	**6< age≤ 12 (n= 64)**	**Total (n=190)**
Cow's milk	37.5	28.5	23	23.4	50
Tomato	16.6	19	5.1	28.1	36
Egg white	37.5	17.4	15.3	3.1	28
Egg yolk	33.3	12.6	7.6	7.8	24
Beef	12.5	17.4	2.5	14	24
Almond	16.6	9.5	5.1	14	21
Tuna	4.1	11.1	12.8	9.3	19
Walnut	12.5	7.9	7.6	10.9	18
Orange	4.1	12.6	5.1	9.3	17
Soybean	16.6	9.5	5.1	4.6	15
Grape	4.1	6.3	5.1	6.2	11
Garlic	4.1	4.7	2.5	6.2	9
Pea	8.3	7.9	0	3.1	9
Wheat	4.1	3.1	2.5	4.6	7
Hazelnut	0	3.1	2.5	6.2	7
Melon	4.1	3.1	0	6.2	7
Potato	8.3	3.1	0	3.1	6
Cabbage	4.1	0	5.1	4.6	6
Corn	0	3.1	0	4.6	5
Onion	0	0	0	7.8	5
Apple	0	3.1	0	3.1	4
Peanut	4.1	0	2.5	1.5	3
Shrimp	4.1	0	2.5	1.5	3
Rice	0	0	0	1.5	1
Mushroom	0	0	0	0	0

*Data are given as percentage

Cow's milk, egg, tomato and nuts were the most common food allergens in different ages. Totally, cow's milk and tomato were the most common food allergens in this study.

DISCUSSION

The incidence of FA in children is higher than in adults. Up to 8% of children less than 3 years of age and 2% of adults suffer from FA (6). The complications due to FA can prevent child growth and even it can be life threatening (5,23), so children with FA should follow a restricted diet, which may lead to parent-child conflict (38). Therefore it is very important to find out the best diagnostic and treatment means and identification of the most common allergens as a priority in every population.

According to the patients' age, common food allergens were categorized into four groups (Table 1). In all age groups the most common food allergens were cow's milk, egg, tomato and nuts. Cow's milk, egg, soy, and wheat allergies have decreased with

increasing age, but tomato, nuts, tuna and orange allergies have increased, which might be due to dietary changes. Although most food allergies gradually improve after three years of age, cow's milk allergy continues till adolescence in 20-25% of patients(39), which is observable in this study, too. Contrary to other studies (40,41), tomato is a common allergen in Iran. Tomato is introduced to Iranian children's food very soon and it is commonly used to make soup for infants that can explain the high prevalence of tomato allergy in Iranian children. In France (11), Japan (12) Israel (13), Australia (40) and Spain (41) egg has been reported as the most common food allergen, but in this study egg was in the second rank or even lower in all age groups. According to many studies walnut is not a common food allergen (33, 42), while in this study it is one of the common food allergens, which may be due to its high consumption in Iranian diet. Contrary, peanut that has been reported as a common food allergen in different studies (35,43-45) has low prevalence in Iran, which is possibly because of its low usage in Iranian staple diet. As discussed above, it is obvious that food habits can influence the type of FA and local experiences should be taken into consideration to diagnose and treat FA in any population.

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