Specific IgE to Common Food Allergens in Children with Atopic Dermatitis

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ABSTRACT

Background: Atopic dermatitis is a major public health problem, often starting in early childhood and sometimes followed by other allergic diseases. Although hypersensitivity to foods is assumed to play an essential role in the development of atopic dermatitis in some patients, little is known about common food allergens in Iranian children with atopic dermatitis. **Objectives:** This study was designed to identify probable food allergens in Iranian children with atopic dermatitis and find the relationship between food sensitization and the severity of atopic dermatitis. **Methods:** This study included 90 children aged 2-48 months with atopic dermatitis. Skin prick tests for cow's milk, hen's egg, almond, potato and soybean were done. Serum specific IgE to 20 food allergens was also screened. **Results:** Among children with atopic dermatitis, the frequency of food sensitization was 40% by skin prick test and 51% by food-specific IgE. Children with atopic dermatitis were most commonly sensitized to cow's milk (31%), hen's egg (17.7%), tree nuts (17.7%), wheat (12.2%), potato (11.1%), tomato (8.8%) and peanut (8.8%). In 42 children with moderate to severe eczema, sensitivity to food allergens was 78.5% by skin prick test and 88% by serum specific IgE evaluation. **Conclusion:** Our results showed that cow's milk, hen's egg and tree nuts were the most common food allergens in Iranian children with atopic dermatitis. Sensitization to foods was much higher in patients with moderate to severe atopic dermatitis. Determining specific IgE in children with atopic dermatitis can be helpful in managing these patients.

Keywords: Allergens, Atopic Dermatitis, Skin Prick Test, Specific IgE

INTRODUCTION

Atopic dermatitis (AD) is a common multifactorial disease which is IgE-mediated in one-third of the patients (1). Increased IgE levels are determined by skin prick testing (SPT) or measuring serum specific IgE (2).
The allergens that most frequently induce hypersensitivity in children are food allergens.

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In a series of experiments, Walzer et al. explained that food allergens can be absorbed via the gastrointestinal barrier and transported to the circulation, where they bind to IgE-bearing skin mast cells and lead to inflammation through the release of potent inflammatory mediators and cytokines (3,4). Sampson et al. demonstrated a high prevalence of food sensitization in children with AD (5). However, there are wide variations in the patterns of food allergens in different countries (6). To diminish AD symptoms, parents often prefer to restrict some foods which may be essential for growth. About 40% of children with moderate to severe AD have been shown to have IgE-mediated clinical reactivity to food proteins (7).
This study was designed to identify probable food allergens in Iranian children with AD and to shed light on the relationship between food sensitization and the severity of AD.

MATERIALS AND METHODS

Patients. This cross-sectional study was performed on children with AD who were referred to an allergy clinic at a university hospital. Ninety children (42 girls, 48 boys) with AD were included in this study to evaluate suspected food hypersensitivity, after informed consent was obtained from their parents and after approval of the study protocol by our university's ethics committee. Atopic dermatitis was defined according to the criteria of Hanifin and Rajka (8). The severity of patients' eczema was scored according to the SCORAD index with assessment of extension items, intensity criteria and subjective parameters. A SCORAD index $\leq$25 was considered mild and an index of 25-103 was considered moderate to severe AD (9). A family history of smoking and exclusive breast-feeding during infancy were recorded for each patient.
Evaluation of Specific IgE. Commercial food extracts including cow's milk, hen's egg, almond, soybean and potato (Stallergenes, Antony, France) were administrated on the forearm in SPT. Normal saline and histamine (10 mg/ml) were used as negative and positive controls, respectively. The results of the skin tests were examined after 15 min and considered positive or strongly positive when the wheal diameter was $\geq$3 mm or 10 mm greater than the negative control, respectively.
Topical corticosteroids (one day) and systemic antihistamines (seven days) were stopped before the skin test. No patient was taking systemic corticosteroids.
Serum was obtained at the time of the initial visit to determine food-specific IgE based on an enzyme immunoassay with 20 allergens including hazelnut, peanut, almond, walnut, milk, egg yolk, egg white, casein, celery, carrot, tomato, potato, cod fish, crab, orange, apple, wheat flour, rye flour, sesame and soybean (R-Biopharm AG, Darmstadt, Germany). The patient's serum was incubated with a nitrocellulose strip prefixed with a horizontal array of allergens. The presence of specific IgE was determined semiquantitatively with enzyme-conjugated anti-human IgE and the corresponding chromogenic substrate. The membrane was scanned and the result was evaluated with specific software. Specific IgE titers at levels of 0.35 kAU/L or higher were considered positive.
We compared the results between two age subgroups of less than 1 year and those aged 1-4 years.
Statistical Analysis. Statistical analysis was done with the chi-square test using version 6 of Epi Info. $p<0.05$ were considered statistically significant.

RESULTS

Ninety children (2-48 months, mean age 20.6 ± 13.3 months) with AD were enrolled in the study. A positive skin test to at least one of the applied food allergens was seen in 40% of the children. Figure 1 shows the rate of positive reactions to five food extracts by SPT in children with AD. As shown, the most frequent sensitizations were to cow's milk (24.4%) and hen's egg (20%). Strong positive skin reactions were observed in five patients to cow's milk (in two children) and hen's egg (in three children).

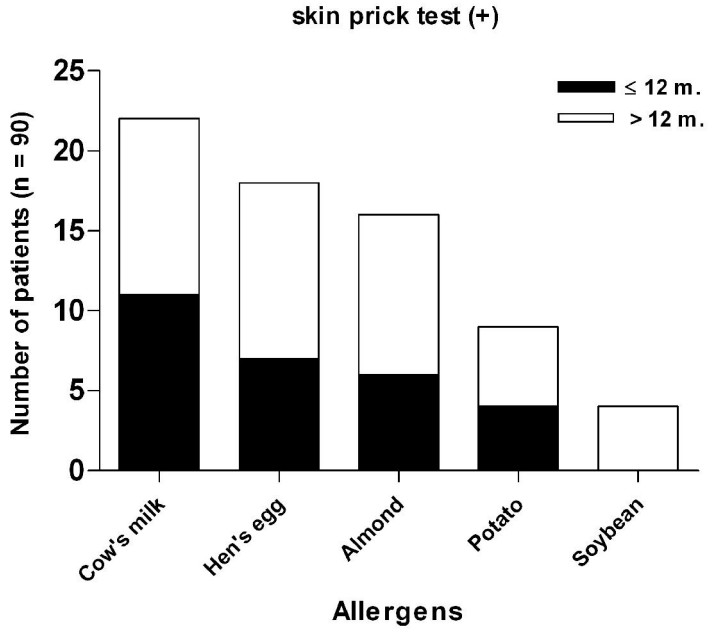

Figure 1. The frequency of positive skin prick test to five commercial food extracts in children with atopic dermatitis, a comparison between the children under and above one year.

Food sensitization was also measured by serum specific IgE to 20 food allergens. Specific IgE to the allergens was observed in 51% of the patients. Figure 2 compares the sensitization to five food allergens by SPT and the presence of specific IgE. Cow's milk sensitization was detected in 28 patients (31%), 5 of whom had an IgE level >3.50 kAU/L. Specific IgE to milk was detected in 9 children with a negative SPT to cow's milk (concordance rate=67%). Specific IgE to egg white was detected in 16 patients (17.7%), only 2 of whom were also sensitized to egg yolk. Specific IgE was not detected in 5 children with a positive SPT to hen's egg (71% concordance). Ten children had concurrent sensitization to both cow's milk and hen's egg.

The results of positive sensitization to almond were similar in the SPT and specific IgE tests (7.7%). Specific IgE ≥0.35 kAU/L to tree nuts (hazelnut, almond and walnut) was detected in 16 (17.7%) children, and positivity for peanut was detected in 8 (8.8%) children.

As shown in Figure 3, serum specific IgE to food allergens was detected in 12.2% of the

participants for wheat, 8.8% for rye meal, 8.8% for tomato, 7.7% for sesame, 7.7% for carrot, 7.7% for celery and 4.4% for orange. Specific IgE to seafood (crab and cod fish) was observed in 3 children. Among the allergens studied here, sensitization was least frequent to apple and seafood (3.3%).

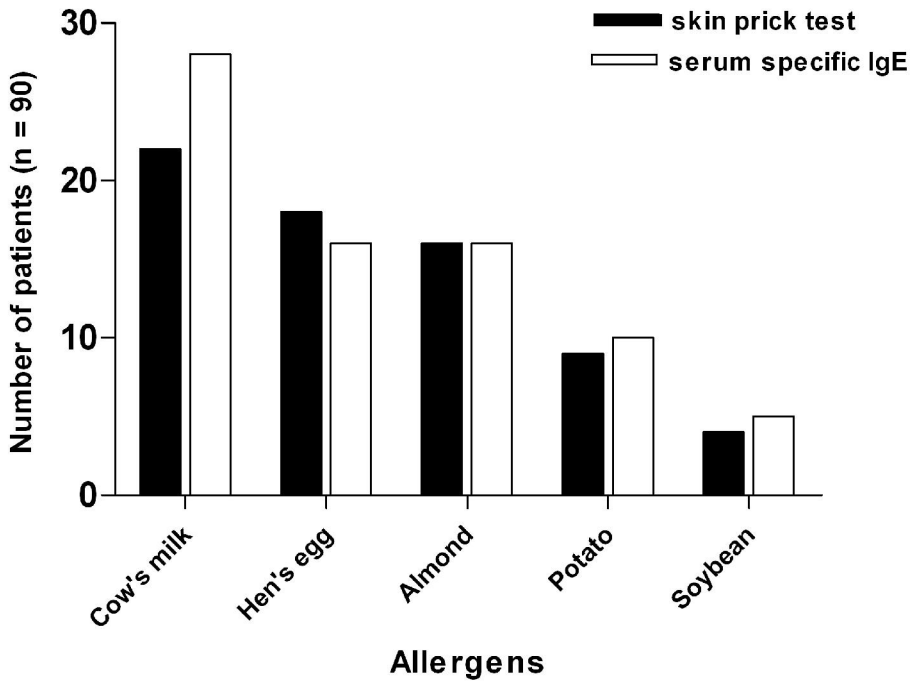

Figure 2. Comparisons of sensitization to five food allergens by skin prick test and in vitro analysis of serum-specific IgE.

Fifty-nine patients (65.5%) with AD had a family history of atopic disorders, and 77 AD patients (85.5%) had a history of exclusive breast-feeding. These factors were not shown to affect the severity of AD in this study.

Among 42 children (46.6%) with moderate to severe AD, 37 (88%) had specific IgE to food allergens and 33 (78.6%) showed sensitivity to food allergens by SPT. Children with a high SCORAD index demonstrated higher rates of food sensitization either by SPT ($p < 0.001$) or tests for the presence of specific IgE to food allergens ($p < 0.001$). This subgroup of the patients was also sensitive to cow's milk (24/42) and hen's egg (14/42).

Thirteen (15.5%) of the AD patients belonged to families in which at least one member was a smoker, and in 9 of them we detected specific IgE to at least one of the food allergens in the panel.

Food sensitization in AD patients aged less than 1 year did not differ significantly from older patients. Moreover, no sensitization to sesame, tomato, crab, and cod fish, orange and apple was observed in any of the AD patients younger than 1 year (36 participants).

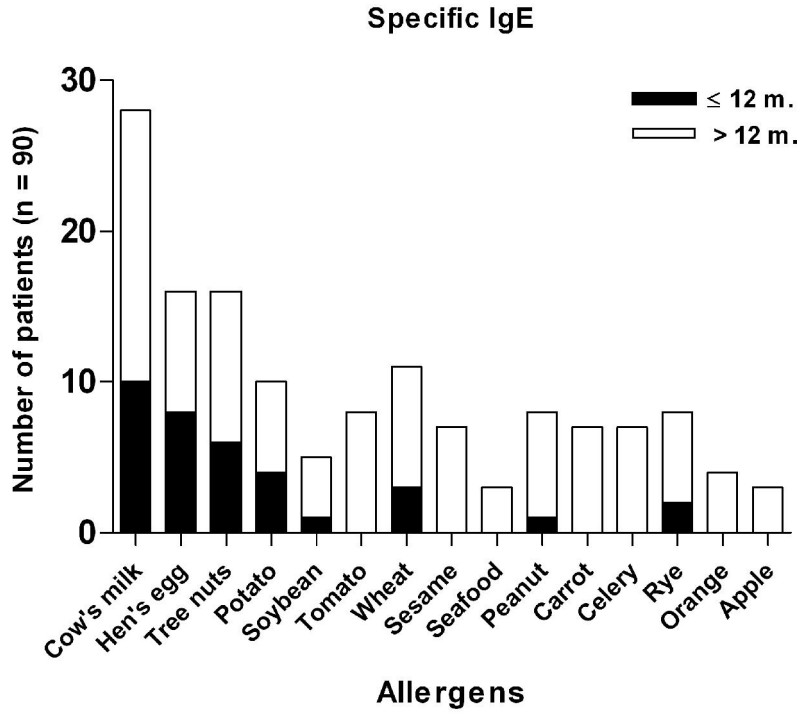

Figure 3. Sensitization to food allergens in under and over 1year old patients with atopic dermatitis based on serum-specific IgE.

DISCUSSION

Concurrent food allergy and AD are significant burdens in the pediatric population, and the incidence of both has been increasing (10). According to the International Study of Asthma and Allergies in Childhood, the prevalence of AD in Iran and China is less than 2%, compared to 20% in Australia and the UK (11). The role of foods in AD was recently clarified, and the results of the present study are further evidence of food sensitization in children with AD (40%-50%). The highest prevalences of sensitization to food allergens are reported in Australia (83%) and the UK (6). The lower incidence of AD alone and concurrently with food sensitization in Iranians may be explained by their genetic background; however, the effect of environmental factors is indubitable.

Although both SPT and in vitro analyses of specific IgE are used to determine immediate allergic reactions, the results of the two tests are often not entirely consistent with each other because of the greater specificity of the former and higher sensitivity of the latter. In the present study, concordance between the SPT and specific IgE results for the five food allergens we tested was 78%, a figure similar to that in a report from Egypt (12). Nonetheless, the combination of SPT and specific IgE remains useful for identifying potential food allergens, although complimentary analysis by double-blind placebo-controlled food challenge is recommended.

The relation between the size of the wheal in SPT and clinical symptoms to a certain food allergen is controversial (13,14). However the results of SPT in our study showed five strong positive reactions to cow's milk (in two children) and hen's egg (in three children). Preferably, the relation between strongly positive skin reactions should be supported by food challenge.

In Australian children with AD, sensitization to egg (54%) and cow's milk (34%) were most common according to sensitization tests (6). The same order of frequency of food allergens was also reported in AD patients from France, Spain, Italy and Korea, although the actual rates were lower (6,15). In contrast, the results of the present study showed cow's milk (31%) to be the most frequent type of sensitization in children with AD, followed by hen's egg (17.7%). Pourpak et al., who used SPT, found that in Iran, the most common food allergies in patients with AD were those to cow's milk (44.5%), tomato (29.41%), egg (28.57%) and nuts (9.24%) (16). Dissimilarities of the order of frequency of common food allergens among different countries can be explained by the interaction of genetic factors, local diet and dietary habits. In these settings, consuming new food preservatives and additives may be among other important causes.

Guillet and Guillet reported a higher prevalence of food allergy among patients with severe AD (17). The results of the present study also confirmed the correlation between food sensitization and AD severity. We found that approximately one third to one half of the children with moderate to severe AD had food sensitization according to SPT and specific IgE analysis.

The role of passive tobacco exposure in AD is uncertain (18). In our patients, we found no correlation between passive smoking and AD. Food sensitization was similar in children who were and were not breast-fed in this study. Although breast-feeding during the first months of life seems to reduce the development of AD, exclusive breast-feeding was not associated with a lower rate of food sensitization in the children we studied (19). This might be explained by the presence of food allergens in breast milk.

We observed no significant difference in the frequency of sensitization to two common foods in patients less than 1 year old and those aged 1-4 years. Further research on food sensitization in early infancy would shed more light on this problem. Particular attention should be paid to children with both food allergy and AD, as these patients are going to be more susceptible to allergic rhinitis and asthma in the future.

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