Original Article

Food Hypersensitivity as a Cause of Atopic Dermatitis

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Abstract Thirty children from infancy to 12 years suffering from atopic dermatitis were evaluated for food hypersensitivity by means of history, skin prick test, total eosinophils count, and elimination of suspected food. Sixteen (53%) patients had history of allergy to suspected food, the other 16 (53%) had other allergic diseases. Of the 30 patients, 15 (50%) had one of the parents with allergic diseases, and in 3 patients both parents suffered from allergic diseases. Nineteen (63%) children had atopic dermatitis triggered by food; egg accounted for 40%, fish for 53% and shrimp for 40% for the allergic manifestations. Skin prick test consisted of 20 food allergens was done to all children above 2 years of age, 12 (40%) of the patients showed positive results. This study demonstrated that food hypersensitivity may play a pathogenic role in some children with atopic dermatitis. Appropiate diagnosis and restriction of diet can improve their skin symptoms. **[Paediatr Indones 1994; 34:129-135].**

Introduction

Atopic dermatitis commonly occurs in all age group, beginning in infancy and early childhood. This skin disorder is characterized by a typical distribution, extreme pruritus, erythema, papulovesicular, intensely pruritic rash, chronically relapsing course, and is associated with asthma and/or rhinitis.[1]

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This disorder is believed to account for 1% of all office visits to pediatricians and to affect from 1.1% to 4.3% of pediatric population. There is evidence to suggest the role of IgE-mediated hypersensitivity in the pathogenesis of atopic dermatitis; some of them are:

1. Approximately two thirds of children with atopic dermatitis have positive family history of atopic disease;
2. Fifty to 80% of children with atopic dermatitis develop allergic rhinitis or asthma;[2]

3. Serum IgE concentrations are elevated in about 80% of children with atopic dermatitis;[3]
4. Most children with atopic dermatitis have positive immediate skin tests and radioallergosorbent tests (RAST) to various dietary and environment allergens.[4]

The pathogenic role of food hypersensitivity in atopic dermatitis has been disputed for nearly a century. In a recent study, however, approximately one third of children seen in university dermatology and allergy clinics showed that food hypersensitivity contributed to their skin symptoms.[1,5] Approximately 60% out of these patients had a positive reaction to double-blind, placebo-controlled food challenge to one of the food allergens tested. In Sampson's study[6] a link between immediate food hypersensitivity and skin symptoms in some children with atopic dermatitis was proven when 14 of 26 children were found to develop cutaneous erythema and pruritus shortly after ingestion of food antigen administered in a double-blind food challenge.

The aim of this study was to determine whether immediate food hypersensitivity plays a part in the pathogenesis of atopic dermatitis in a pediatric population and, if so, whether skin testing is useful in the diagnosis of hypersensitivity reactions in these patients.

Methods

Thirty children from infancy to 12 years old referred for evaluation of atopic dermatitis between November 1987 and December 1992 were enrolled in the study. All subjects had a history of atopic dermatitis which was defined as a pruritic, chronic or chronically relapsing, non-infectious dermatitis of typical morphology and distribution suggested by Hanifin and Lobitz.[3] Most were managed with topical steroids, antihistamines, or systemic steroids. The eczema was regarded as severe if it was generalized and/or if there was a need for hospitalization, as moderate if localized and required frequent application of steroid ointments, as mild if no or only mild steroid ointment was needed for 1-3 days.

For the purpose of this study we evaluated 30 children using a standard questionnaire, skin prick test (SPT) and determination of total eosinophils. An episode of bronchial obstruction was accepted only when the diagnosis was made by a physician, and three or more episodes of bronchial obstruction were regarded as asthma. Rhinitis was considered to be allergic if it appeared at least twice after exposure to a particular allergen(s). Positive exposure to an allergen was defined as an obvious reaction within one hour after exposure in at least in two occasions.

Skin prick tests were performed on the volar aspects of the forearm in all children by using a battery of 20 different food antigens. Standard glycerinated extracts from Dome-Hollister Stier in a concentration of 1:20 (weight/volume) were applied by the prick technique; the mean diameters of the erythema and wheal reactions were subsequently recorded. The result was intepreted as follows: diameter of wheal reaction of 3 mm or more than that of the control subjects was considered positive.

If no more than a few foods were suspected as the cause of symptoms, the initial elimination diet consisted simply of removing these foods. If removal of one or several foods from the diet was not successful in eliminating the symptoms, initiation of a severely limited diet for a short periods of time was done, followed by the return of each suspected food three weeks later. Continuation of symptoms while patients were on restricted diets indicated that the symptoms were not caused by food.

Results

Thirty children, 15 males and 15 females were enrolled in the study (Table 1). The patients ranged in age from 4 months to 12 years. The family history was positive for atopic disorders (allergic rhinitis, asthma, atopic dermatitis) in 18 (60%) of the patients. History of atopic disorders in one of the parents was found in 15 (50%) of the patients, while history of atopic disorders in both parents was found in 3 (10%) patients (Table 2).

Table 1. Age and sex distribution of children with atopic dermatitis

Age group (years)	Male	Female	Total
0-	2	-	2
1-	2	7	9
2-	4	4	8
5-	4	4	8
10 or more	3	-	3
Total	15	15	30

Table 2. Distribution of atopic disorders in 30 patients by age

History of allergy	Age (year) 0-	1-	2-	5-	10 or more	Total
1 of parents	1	3	4	6	1	15 (50%
Both parents	-	1	1	-	1	3 (10%)
None	1	6	2	2	3	12 (40%)

Table 3. History of other allergic diseases in 30 patients

	0-	1-	2-	5-	10-	Total
Asthma	-	2	1	2	1	6
Rhinitis	-	-	1	1	2	4
Asthma and rhinitis	-	-	1	1	2	4
Urticaria	1	-	-	-	-	1
Asthma and urticaria	-	-	1	-	-	1
None	2	5	3	4	-	14

In addition to atopic dermatitis, 6 children had asthma, 4 had allergic rhinitis, 4 had both allergic rhinitis and asthma, 1 had urticaria, and another patient had both asthma and urticaria. In 14 of children with atopic dermatitis no history of any other allergic disease was elicited. See Table 3.

Skin prick tests were not done in 11 infants and children under 2 years of age due its notorious unreliable results. The results of the test in the remaining 19 children were as follows (Table 4):

Table 4. Results of skin prick test to a battery of 20 food allergens in 19 patients age 2-12 years old with atopic dermatitis

Food allergen	Positive reaction
1. Egg	6
2. Shrimp	4
3. Fish	3
4. Chocolate	3
5. Peanut	2
6. Crab	2
7. Strawberry	2
8. Milk	1
9. Wheat	1
10. Chicken	1
11. Pork	1
12. Beef	0

Of the 19 skin tests performed, 12 yielded positive reaction. Egg gave positive result in 6, shrimp in 4, and fish in 3 patients.

Table 5. Food inducing positive challenge in 19 of 30 children with atopic dermatitis

	0-	1-	2-	5-	>10	Total
1. Egg	-	2	4	1	1	8
2. Fish	-	3	3	3	1	10
3. Shrimp	-	-	3	4	1	8
4. Crab	-	-	2	2	-	4
5. Egg & fish in breastmilk	1	1	-	-	-	2
6. Chicken	-	-	1	-	-	3

A total of 24 elimination diet and food challenge children were undergone, 6 based on history only, because they did not come back for follow-up; 19 (2 based on history) were interpreted as positive.

Agreement between oral challenge tests and the results of skin tests was found in 5 out of 19 patients. The onset of symptoms usually occurred within 4-6 hours of ingesting food antigens and no significant delayed reaction were noted. The skin symptoms which were seen mostly were diffuse erythematous macular or morbilliform rash and pruritus.

Eleven foods accounted for all positive challenge and/or history. Of these children, 7 patients were positive to 1 kind of food, 4 patients were positive to 2 kinds of food, 3 were positive to 3 kinds of food, 5 were positive to 4 or more kinds of food. Egg accounted for 40.6%, fish for 52.6%, and shrimp for 40.6%.

Discussion

The clinical significance of food hypersensitivity in atopic dermatitis has been debated for many years, but increasing evidence suggest a pathogenic role for IgE-mediated hypersensitivity mechanism. Sampson and McCaskill[6] show that food play a pathogenic role in some children with atopic dermatitis. Approximately 60% of children challenged have a positive food reaction.

Engman et al[6,18] suggested in 1936 that the ingestion of food might play a role in the exacerbation of atopic dermatitis. They hospitalized a child with wheat hypersensitivity who remained on a wheat-free diet until his skin symptoms were clear. After the symptoms were clear, the child was allowed to consume wheat in his diet. This challenge resulted in severe scratching and typical lesions of atopic dermatitis. These studies and others suggest that food does participate in exacerbating dermatitis.

The lesions are considered to be the consequence of immediate IgE-mediated food hypersensitivity producing a pruritic rash, after ingestion of an offending allergen, which leads to severe scratching, lichenification, and typical skin changes in atopic dermatitis.

The proposed mechanism by which adverse food reactions exacerbate skin symptoms is the late-phase IgE response. Two to 4 hours after ingestion of antigen there is a progressive accummulation of eosinophils and neutrophils, which reach a maximum concentration at six to 8 hours, and skin symptoms which are heralded by pruritus and consisted of an erythematous macular or morbilliform rash follows.

More evidence suggests that other mediators released during IgE hypersensitivity responses, such as mast cell-derived prostaglandin and leukotrines or eosinophil "major basic protein" may also contribute to the skin changes seen.

A child (especially those younger than 7 years) with atopic dermatitis unresponsive to routine therapy (topical steroids, antihistamines and occasional systemic steroids) appears to have greater than a 50% chance of having food hypersensitivity.[7] Such children should therefore undergo appropriate evaluation.

In the past, and even more recently, some investigators have suggested that children with atopic dermatitis are allergic to a wide variety of food antigens. This statement generally is based on the results of skin tests or RAST tests, clinical impressions, or dietary exclusion and challenge studies.

Many of our patients had positive skin prick test reaction to several food antigens; 36.8% of the children experienced positive oral challenge to only 1 food, 21% to 2 foods and 32.1% to 3 foods or more. While skin prick test showed that egg accounted for 50%, shrimp accounted for 33%, and fish to 25%, oral food challenge showed that egg accounted for 40.6%, fish for 52.6% and shrimp for 4.6% and only five of out 19 patients (26.3%) positive for food challenge demonstrated a positive skin prick test to the same food.

Most scientists agree that the most appropriate mean in diagnosing food hypersensitivity in patients having atopic dermatitis starts with a careful medical history and physical examination directed at distinguishing food hypersensitivity from other causes of adverse reactions to food. Skin tests and *in vitro* tests for antigen-specific IgE are used in selected cases to support the clinical diagnosis. Confirmation of the diagnosis may be obtained by oral elimination and challenge with suspected food.

Before any diet is initiated, it is useful for the patient to remain on the usual diet for 1 to 2 weeks. During that time the parents record the type and amount of food ingested and the occurrence and characteristics of food reactions. If no more than a few foods are suspected as the cause of symptoms, the initial elimination diet can consist simply of removing these foods. If removal of one or several foods from the diet is not successful in eliminating symptoms, if multiple food

sensitivities are suspected, or if the symptoms are unlikely to be caused by food, initiation of a severely limited diet is sometimes warranted. Severe elimination diet, especially in children, can be used for only a short period of time. Extensive elimination diet for infants under 3 months of age including milk substitute alone and elimination of the mother diet; 3-6 months of age, milk substitute and rice cereal; 6 months to 2 years milk substitute, cereals, certain fruits, eggs, chocolate and peanuts. Continuation of symptoms while patients are on restricted diet indicates that the symptoms are not caused by foods.

If symptoms resolve on the restricted diets, provocation can be started 3 weeks later, and all symptoms provoking foods should be removed. Although the procedure described is lengthy, it is direct and applicable to patient evaluation with a minimum confusion.

A number of *in vivo* and *in vitro* techniques procedures have been used in the diagnosis of food allergy. These techniques include skin testing, RAST and ELISA. Skin prick testing may be considered as an excellent mean of excluding IgE-mediated food allergies but is only suggestive of the presence of clinical food allergies with some exceptions. First, IgE-mediated sensitivity to a great number of fruits and vegetables is frequently not detected because of the lability of the responsible allergen.[5,8] Second, children less than 1 year of age may have IgE-mediated food allergy in the absence of positive skin test result and infants less than 2 years of age may have a smaller wheals, presumably because of a lack of skin reactivity. Third, individuals may have positive skin tests in the absence of food allergy (false positive) and allergy to food in negative skin tests (false negative). Patients should never be advised that they are allergic to certain foods solely on the basis of skin tests.[5]

Radioallergosorbent tests (RAST) and similar *in vitro* assays such as enzyme-linked immunosorbent (ELISA) assays are considered slightly less sensitive than skin prick tests.[1,5] One study that compared Phadebas RAST (Pharmacia AB, Uppsala, Sweden) with double-blind, placebo controlled food challenges found skin prick tests and RAST's have similar sensitivity and specificity when a Phadebas score of 3 or greater was considered positive. Oral food challenge (double-blind food challenge) may be used occasionally for the diagnosis of food intolerance if the correlation between specific foods and symptoms remain unclear. It need not be used if the medical history, physical examination, skin testing and dietary studies have resulted in diagnosis. Though double-blind placebo-controlled food challenge provides a scientifically acceptable way of diagnosing adverse food reactions, such challenge may be impractical for general clinical use.[6]

In conclusion, in some children food hypersensitivity does play a pathogenic role in atopic dermatitis. This hypersensitivity to food is generally limited to one or two antigens and may be lost after several years. Appropriate elimination diets should not pose the nutritional hazard. Children who are appropriately diagnosed and given restricted diets can be expected to show significant improvement in their clinical course. Skin testing with the prick technique may be of some aid in diagnosing food allergy, but a high rate of clinically insignificant positive skin tests and a small rate of false negative test occur.

In some children whom food hypersensitivity cannot be documented, other factors such as temperature extremes, stress, contact with house dust mite, animal dander, possibly pollen allergens and unknown factors should be considered.

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