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Is food allergy testing reliable in pediatric atopic dermatitis? A population-based study

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Abstract

We sought to assess the value and reliability of serologic testing for predicting clinical food allergy in a population-based cohort of infants with atopic dermatitis (AD). Infants 3–18 months of age, recruited from the general population, were followed quarterly for three years and carefully evaluated for evidence of immediate reactions to foods. Specific serum IgE levels for six foods were assayed at 3–5 years. Parents were interviewed at each visit regarding past and current immediate food-specific reactions involving skin, gut or respiratory systems. Data were entered into Excel for calculations of performance e characteristics. Nine of the 40 patients (23%) who completed three years of follow-up had reactions to one or more foods. Reactions occurred in 5, 11, and 18% to milk, peanut and egg ingestation, respectively. In contrast, 30% of food-specific serum IgE tests were above normal. Predictive reliability of tests was generally low unless values were in the high range for peanut and milk. Conversely, egg allergy could be seen across a nearly full-spectrum of IgE values, making prediction highly unreliable. We conclude that physician and patient misinterpretation of the relevance and reliability of allergy testing may misdirect proper prevention and therapy of atopic dermatitis.

During the past century, the association between IgE reactivity and atopic dermatitis (AD) led to an assumption that food allergy was a causative factor. In recent years, an alternative concept has arisen, suggesting that food-specific IgE reactivity may be a secondary phenomenon caused by excessive transcutaneous absorption of antigens through a dysfunctional stratum corneum barrier (1,2). The concept was greatly strengthened by studies showing the strong association between filaggrin mutations, ichthyosis vulgaris, AD and asthma (3).

Well-documented food allergy prevalence among children with AD in university clinics is roughly 30%, but because of weak and inconsistent diagnostic criteria, reports may cite frequencies of 60–80% (2,4). Only distinct type I reactions occurring within 20–120 minutes of food ingestion clearly confirm the presence of food allergy. Confusing the issue are claims that a variety of delayed skin symptoms and lesions, including eczema flares and morbilliform rashes one to four days later, result from food allergy. The predictive reliability of IgE testing to foods is controversial, with values often reported as “low” to “very high” and varying with patient age and underlying health conditions (5–7). Our objective was to evaluate the predictive reliability of food-specific IgE testing in a population-based cohort of children 3–5 years of age with AD.

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Methods

Infants 3–18 months of age with mild-to-moderate AD – but no history of food or respiratory allergy – were recruited from the general population. Specific serum IgE levels for six foods (ImmunoCAP) were determined as baseline and after three years. Parents were interviewed quarterly regarding known exposures to each of the tested foods and for any reactions within 30–120 minutes of ingestion. Delayed or indeterminate reactions (e.g., eczema flares, constipation) were not accepted as indicators of allergy.

Severity of AD was quantitated by EASI score. IgE levels were considered elevated if >0.34 kU/l (5). Data were entered into Excel for calculations (SPSS was used to assess correlations).

Results

A total of 88 subjects were initially screened and 40 completed three years, at which time 90% or more had ingested each of the six food antigens studies (Table 1). Nine children had immediate type clinical reactions, consistent with true food allergy, after ingestion of one or more foods. These included reactions from exposure to egg white in 7 of 38 (18%), peanut in 4 of 37 (11%) and milk in 2 of 39 (5%). No child reacted to wheat, soy or fish, or any other foods during the three years of the study. Of the 240 tests performed after three years on study, 71 (30%) showed specific IgE above the normal level (0.34 kU/l). Even the three children who had never been known to ingest peanuts had increased peanut-specific IgE ranging from 0.70 to 18.00 kU/l (mean: 7.56 kU/l), suggesting possible transcutaneous exposure (2).

We categorized specific IgE values into “definitely allergic,” “possibly allergic” and “nonallergic” using Sampson’s risk predictions (5) (Table 2). Values varied widely, leaving risk uncertain over an extensive range from low to “definitely allergic” ranges. Patients with egg allergy were most unpredictable, ranging from 0.38 to 48.6 kU/l and levels for 4 of 7 egg-allergic patients were well below the 95% prediction level from many studies (5–8). Values in our two milk-allergic children were very high, in the “definitely allergic” range, while none of the 14 in the “possibly allergic” range reacted to milk. Overall, IgE values in the “possibly allergic” realm among our allergic patients were not indicative of allergy except for egg. Thus, 90% of values might have been wrongly assumed to be allergy. Regarding overall prevalence of elevated serum IgE in our cohort, we calculated the percentages in the normal, “possibly reactive” and “reactive” ranges of IgE (5). Values indicated that only 11–50% of AD children have elevated IgE levels for the six common food allergens and, as mentioned above, even fewer showed true allergy.

Discussion

Food allergy has become a high-impact concern in many Western countries. News stories banner case reports and medical providers focus on using tests and dietary avoidance strategies. Industries, including allergen producers, laboratory test manufacturers, and probiotic and hypoallergenic formula makers, all profit from the food allergy obsession. Misrepresentations are fueled by studies selected for severe AD patients in tertiary care centers and by reports implying that diagnostic criteria such as IgE tests and eczema flares are reliable indicators of food allergy. Our study profiles young children selected for treatment of AD, a group typically seen in dermatology and pediatric clinics, contrasting greatly with the many studies in selected children (5–11). Our results suggest that diagnoses and prevalence estimates of relevant IgE sensitization and actual food allergy in infants and children with AD may be considerably inflated.

Another misapprehension from studies in AD is the belief by many that food allergy is an important causative factor for AD. Such correlative claims are not borne out by our study. Roughly 80% of our children had neither serologic nor clinical evidence of food allergy. Most patients with elevated serum IgE levels had mild eczema, easily controlled with topical care. Causative misperceptions are fueled by the frequently positive skin tests and elevated serum IgE levels that may be secondary to AD barrier defects. It is reinforced by reports of eczema improvement with food restriction (11), although all agree that the natural course of AD is improvement during childhood and that restrictive diets are diagnostically unreliable (12). Allergic causation of eczema is a strong belief among allergists, primary care physicians, and alternative practitioners, which leads to extensive and often unnecessary allergy testing and, in turn, greatly amplifies the public concern about food allergy.

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Table 1

Frequency of elevated food-specific IgE levels and immediate allergic reactions among children with AD.

Food	Never exposed, n (%)		Exposed, n		
	Total	With increased IgE (%)	Total	With increased IgE (%)	With allergy (% exposed)
Peanut	3	3 (100)	37	10 (27)	4 (10)
Egg	2	1 (50)	38	18 (47)	7 (18)
Cow milk	1	0 (0)	39	16 (41)	2 (5)
Wheat	0	0 (0)	40	13 (33)	0 (0)
Soy	4	0 (0)	36	6 (17)	0 (0)
Fish	4	0 (0)	36	4 (11)	0 (0)

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Table 2

IgE decision points* compared to reactions in infants exposed to foods.

Allergen (n)	IgE "definitely allergic" kU/l (range)		IgE "possibly allergic" kU/l (range)		IgE "nonallergic" <0.35 kU/l	
	Reported reaction	No reported reaction	Reported reaction	No reported reaction	Reported reaction	No reported reaction
Peanut (37)	4 (26.1 – 73)	0	0	6 (0.47 – 1.01)	0	27
Egg white (38)	3 (7.8 – 48.6)	1 (7.58)	4 (0.38 – 0.71)	11 (0.37 – 3.43)	0	19
Milk (39)	2 (>100)	0	0	14 (0.41 – 2.84)	0	23

*Decision points from Sampson (5).