

Report

Identification of allergens by IgE-specific testing improves outcomes in atopic dermatitis

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doi: 10.1111/ijd.13673

Abstract

Introduction IgE quantitative assaying of allergens (IgEQAA) has long been implemented by allergists in determining patients' reactivities for allergic rhinitis and asthma, two of the three diagnoses in atopic syndrome. This test operates by measuring the patient's IgE response to different allergens and can identify potential triggers for a patient's symptoms. Despite this, IgEQAA has yet to see the same widespread use in the field of dermatology, specifically in the treatment of patients with atopic dermatitis (AD).

Materials and Methods The affected body surface area (BSA) at first presentation, IgEQAA classes, and total immunoglobulin E (IgE) concentration were taken retrospectively for 54 patients with AD.

Results Of the 54 patients observed, 41 had an abnormally high total IgE concentration (76%). Additionally, it was observed that nine (17%) of our patients significantly improved after making lifestyle changes.

Conclusion Knowledge of the identified specific antigens can guide patients to make lifestyle modifications that may improve disease outcomes. IgEQAA and avoidance of allergens may help some patients with AD.

Introduction

IgEQAA is an *in vitro* method of testing for a patient's reactivity to different environmental allergens. It is also known as radioallergen sorbent (RAST) testing, which is quantitative for all individual allergens. Historically, IgEQAA has been used by allergists in the diagnosis and treatment of diseases with known allergic triggers such as allergic rhinitis and asthma because of both IgEQAA's high sensitivity and specificity.¹

The test may be a valid indicator of AD severity as a result of the relationship between immediate hypersensitivity responses and AD. A review by Fuiano and Incorvaia details the specific mechanisms by which dust mite antigens aggravate the symptoms of AD. Direct binding of allergens to specific IgE elicits a typical immunological response, leading to inflammation and cutaneous tissue destruction. Additionally, IgE-mediated histamine release can cause pruritus, further exacerbating the symptoms of AD. Also, Langerhans cells in the skin of patients with AD exhibit a greater concentration of the IgE receptor, FcεRI, than that of the average individual.² A separate review by Wolter and Price states that inherited immune diseases, such as hyper IgE syndrome, are correlated with the early development of eczematous symptoms.³ In an article studying the correlation between castor bean allergy and IgEQAA results, IgEQAA was found to have a 97% correlation with positive scratch tests and a 95% correlation with negative scratch

tests. This high level of reliability, coupled with the low risk of an *in vitro* test, has made IgEQAA a useful tool in the treatment of allergic diseases.⁴ AD has been shown to be aggravated by multiple different environmental allergens, especially certain aeroallergens. In a study conducted by Goon *et al.*, it has been shown that patients with AD tested positive to both atopic patch and IgEQAA testing for house dust mites at a level significantly higher than that of controls.⁵ As aeroallergens such as dust mites are virtually unavoidable, the extent of their impact on patients with atopy is extremely important but difficult to address.

The purpose of the study was to see if there is a correlation between IgEQAA score and AD severity as well as improving clinical outcomes by making lifestyle changes with the knowledge gained. Such a correlation could be clinically relevant as IgEQAA testing may be utilized as an indicator of environmental triggers in patients with moderate to severe AD. Patients may then be able to implement specific allergen avoidance as a method of alleviating the symptoms associated with AD.

Methods

This was a retrospective study of 54 patients from a private dermatology practice.

All patients had undergone total IgE levels and IgE Quantitative Allergen Assay from a predetermined panel of the most

Table 1 Immunocap results table

kU/l	Class	Clinical implications
<0.10	0	Undetectable
0.10–0.34	0	Low level. May represent a risk factor for future sensitization or ongoing sensitization
0.35–0.69	Class 1	Low level. May represent a risk factor for future sensitization or ongoing sensitization
0.70–3.49	Class 2	Moderate level. Likely represents a contributing factor to total allergic load and/or stronger ongoing sensitization
3.50–17.49	Class 3	High level. Indicative of clinically relevant high level sensitization
17.50–49.99	Class 4	Very high level. Indicative of clinically relevant high level sensitization
50.00–99.99	Class 5	Very high level. Indicative of clinically relevant high level sensitization
≥100.00	Class 6	Very high level. Indicative of clinically relevant high level sensitization

Data was analyzed using the Chi-square test and 95% confidence intervals for proportions. The level of significance was set to 0.05.

common respiratory allergen antigens. We evaluated AD severity based on total affected body surface area (BSA) with mild AD having <3% BSA, moderate AD having 3–10% BSA, and severe AD having >10% BSA.⁶ The Immunocap method by Thermo Scientific was used to measure the total IgE and the individual antigens. The test operates by binding antibodies from the patient's blood to a specific allergen. The solution is then washed, and enzyme-linked antibodies are added to the solution. Patient antibody concentration is determined via spectrophotometry. (Table 1).

Results

All patients involved in the study were diagnosed with chronic AD, and the male to female ratio was 32:22. Patient ages ranged from 1 year old to 100 years old, with an average age of 42.9 years. Patients' affected body surface area (BSA) at first presentation ranged from trace levels to 80.5%, with an average of 16%. Total IgE concentrations ranged between 3.4 and 41,469 IU/ml, with an average of 2682.7 IU/ml. (Table 2).

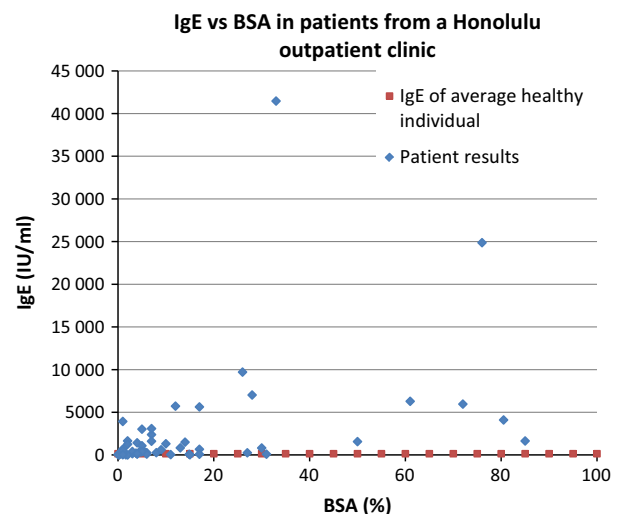
Of the 54 patients observed, 41 (76%) had an abnormally high total IgE concentration of greater than 150 IU/ml (Fig. 1).⁷ The 95% confidence interval for percentage of AD patients with an abnormally high total IgE concentration is 65–87%. Additionally, data was taken from patients who had an IgEQAA class of three or higher in response to certain allergens, and this was compared to their BSAs. Fifteen out of 33 patients who responded to *dermatophagoides farinae* were diagnosed with severe AD; of these patients, seventeen had an IgEQAA class of 6. Sixteen out of 34 patients who responded to

Table 2 Demographics of patients with AD (*N* = 54)

	<i>N</i> (%)	
Gender		
Females	22	(41%)
Males	32	(59%)
Atopic active disease		
AD	49	(90.7%)
AD, Nummular eczema	5	(9.3%)
	Mean (SD)	Median (Min–Max)
IgE results (IU/ml)	2682.7 (6606.5)	638.3 (3.4–41 469.0)
Age* (years)	42.9 (26.4)	47.0 (1–100)

AD, atopic dermatitis.

*Two patients were infants under 1 year of age and are not included in the age statistics.

**Figure 1** IgE vs. BSA in patients from a Honolulu outpatient clinic

dermatophagoides pteronyssinus were diagnosed with severe AD; of these patients, 18 had an IgEQAA class of 6. (Table 3).

One of the patients with severe AD and an IgEQAA class of 6 to mites nearly cleared of his AD when he moved from an older, rundown home to a new condominium. Eight out of 16 patients who responded to dog dander were diagnosed with severe AD; of these patients, two had an IgEQAA class of 6. Four of the 16 patients slept with their dogs and improved when the dog was removed from the bedroom. Six out of 10 patients who responded to cat dander were diagnosed with severe AD; of these patients, one had an IgEQAA class of 6. Four of the 10 were found to have slept with their cats. Three of the six became clear when they limited exposure to cats. None of the patients had repeat IgEQAA levels drawn. Results would not be expected to be significantly different from pre-lifestyle change levels. (Table 4).

Table 3 Relationship between AD severity and IgEQAA class

		Max Class (# of patients)		Total
		Class ≤ 2	Class ≥ 3	
Severity of AD	Severe	4	16	20
	Mild-Moderate	14	20	34
	Total	18	36	54

AD, atopic dermatitis.

While 80% (16/20) of the patients with severe AD had a more severe response (class 3 or greater) to one or more allergens, the association of severe AD with severe response was not statistically significant (chi-square test P -value = 0.1109).

Discussion

IgEQAA testing has significantly impacted the management of atopic disease associated with identification of antigens. The

knowledge gained from this test may have an impact on a significant number of patients with AD. Nine (17%) of the 54 patients reported making one or more lifestyle changes that resulted in significant improvement of their AD without burdensome topical or risky systemic treatments. For most of these patients, their symptoms cleared after making changes in their lifestyle to avoid allergens they are sensitive to. Assuming the extreme case where the other 45 patients attempted to make a change but did not have any improvement, we can consider that 17% of AD patients may be able to improve their AD condition using the test results as a guide to a lifestyle change. The 95% confidence interval for the percentage of such AD patients that may achieve significant improvement is 7–29%. It is possible that only some of the 45 patients without improvement attempted any changes to their lifestyle, and in that case the observed percentage of patients with improvement along with the 95% confidence interval would be minimum estimates. In our sensitized patients, we were able to have a significant impact on outcomes when the patients avoided animal dander,

Table 4 Patient reactivities to different allergens

Allergen of Interest	Number of Patients (%) by Reactivity			
	IgEQAA class ≤ 2	IgEQAA class 3–5	IgEQAA class = 6	Total
Dermatophagoides farinae	21 (38.9%)	16 (29.6%)	17 (31.5%)	54 (100%)
Dermatophagoides pteronyssinus	20 (37.0%)	16 (29.6%)	18 (33.3%)	54 (100%)
Dog dander	38 (70.3%)	14 (25.9%)	2 (03.7%)	54 (100%)
Cat dander	47 (87.0%)	7 (13.0%)	0 (00.0%)	54 (100%)

Table 5 Patients with significant improvement after learning of IgEQAA results

Age	Gender	BSA before treatment	BSA after treatment	Lifestyle change	Total IgE (IU/ml)	IgEQAA results
60	F	5%	Clear	Stopped sleeping with dogs	104	Dog Dander 3+ Dust Mites 2+
58	F	1% (25% of face and neck)	Nearly clear	No facial or neck contact with dog	225	Dog Dander 4+
60	M	76%	Clear	Stopped sleeping with dog	24 825	Dog Dander 6+ Dust Mites 6+
36	M	7%	2%	Avoids contact with dog and dog is not allowed in bedroom	5722	Dog Dander 6+ Dust Mites 6+
55	M	31%	Clear	Moved from old house to new condo	692	Dust Mites 4+
57	M	4% (30% of back)	Clear	Stopped lying in Bermuda grass after exercise	155	Bermuda Grass 3+ Dog Dander 3+ Dust Mites 3+
43	F	2% (50% of face and eyelids)	Clear	Limited exposure to cats/dogs	1251	Dust Mites 5+ Cat Dander 3+ Dog Dander 2+
59	M	1% (25% of face and chest)	Clear	Puts allergy covers on pillows and no longer had contact with dogs/cats	500	Dust Mites 3+ Cat Dander 1+
74	M	1% (25% of face and eyelids)	Clear	Avoided cat	42	Cat Dander 1+

BSA, body surface area.

Bermuda grass, and dust mites. Avoidance of dust mites is a difficult achievement; recommendations include intense cleaning or removal of textiles such as carpets, drapes, stuffed animals, mattress covers, and pillow covers. Even when adhered to, such recommendations have shown mixed results in the decrease of mite allergens and can be expensive and labor intensive¹ (Table 5).

In the treatment of allergic rhinitis and asthma, allergists have used IgEQAA, skin prick testing, and specific inhalation challenge as methods of diagnosing the potential triggers of patients' symptoms.⁸ IgEQAA becomes particularly useful when the specific allergens a patient has been exposed to are not known. IgEQAA may also be able to detect a patient's sensitivity to seasonal allergens before skin prick testing is able to do so. IgEQAA is preferred over skin prick testing in certain circumstances: if anaphylaxis is a significant possibility, if the patient has an aversion to skin prick testing, if the patient's skin is not suitable because of extensive dermatitis, or if the patient is on medications that would interfere with the skin prick test.⁹

A study investigating the role of *Candida albicans* in atopy found that patients with AD were more likely to have a positive immune response to *Candida albicans* mannan than did controls; also, a significant correlation was shown between the severity of the disease and the patients' IgEQAA class.¹⁰

A study conducted by Barnetson, Wright, and Benton illustrates the potential applications of IgEQAA in treating AD. In their study, 12 patients with AD were cat owners. IgEQAA showed that eight patients were highly sensitive to cat epithelium (>100 IU total IgE), and all of them showed some sensitivity to the allergen (at least an IgEQAA class of 1). Findings such as this may indicate a correlation between the patients' cat ownerships and AD, which could be used to direct future treatment.¹¹

In a study conducted by Tanaka *et al.*, patients with AD were found to have a higher IgEQAA class than healthy control subjects in response to eight different allergens. Of the allergens tested, *Dermatophagoides farinae* showed one of the most significant differences, with about 70% of patients with AD having some allergic response to the allergen and only about 15% of the healthy controls doing the same. About 15% of the patients with AD had a class five or six, the highest IgEQAA classes, response to *Dermatophagoides farinae*, while none of the healthy controls had a class six response.¹² As the American house dust mite, *Dermatophagoides farinae* is an allergen that most Americans are regularly exposed to.

Tanaka *et al.* discovered that patients with atopic dermatitis had a higher overall IgE concentration, with a median concentration of 1226 U/ml in patients with AD compared with 71 U/ml in the healthy controls.¹² Our study shows a median IgE concentration of 638.3 IU/ml, a number also significantly elevated

in relation to the average individual. This elevation in IgE concentration indicates a higher overall reactivity to allergens in patients with AD, showing that allergens may play a much larger role in the lives of patients with AD than that of the normal population.

Conclusion

While IgEQAA has historically been used by allergists, it has yet to see the same widespread usage within the field of dermatology. IgEQAA is easy to perform compared to skin prick testing and may be helpful in some patients who are not responding to conservative treatment. Further studies are required, however, from our data it appears that IgEQAA testing can have a significant impact on treatment outcomes in selected patients with AD.

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