Elevated Specific IgE to Bystander Foods in Children with Peanut Allergy

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Abstract

Rationale: Circulating food-specific IgE (sIgE) levels are associated with the development of allergic responses. However, food-specific IgG4 (sIgG4) levels have been associated with tolerance or clinical nonspecific responses, particularly in interventional studies. We aimed to characterize food-specific antibody responses in a more general pediatric allergy population.

Methods: We measured serum specific IgG4 (sIgG4), sIgG, and sIgE to whole peanut, egg, white, and wheat, along with total sIgE, from 57 children (31 with peanut allergy, 6 with wheat allergy, 6 with peanut and egg allergy, and 6 with the Phadia ImmunCAP system.

Results: As expected, total IgE was highest in children with food allergy compared to children without food allergy or naturally tolerant children (p<0.001). sIgG and sIgE levels were highest in children with peanut allergy compared to naturally tolerant and control children (p<0.001, p=0.001, respectively). This indicates that the specific IgG4/sIgG ratio was lower in children with peanut allergy compared to naturally tolerant and naturally tolerant children (p=0.002). Interestingly, children with only peanut allergy had comparable egg sIgG and wheat sIgE levels to children with both peanut and egg allergy. Children with only peanut allergy also had higher levels of egg and wheat sIgE compared to naturally tolerant or control children (p<0.002, p=0.01 respectively). sIgE levels were undetectable in 89% of participants.

Conclusions: Our findings indicate that children with peanut allergy have elevated sIgE to bystander foods that they are eating, suggesting that the mechanisms regulating production of sIgE to foods is dysregulated in these children.

Introduction / Methods

Introduction: Food allergy results from a loss of oral tolerance to ingested proteins and development of food-specific Immunoglobulin E (sIgE), sIgE levels are widely used in clinical practice for diagnosis and longitudinal follow up of patients to monitor development of natural tolerance. However, the value of sIgE in patients without clinical history of reaction is limited and sIgE levels to tolerated foods remain unknown. Data from oral immunotherapy trials (OIT) have shown changes in immunoglobulin isotypes with development of tolerance, particularly increased levels of sIgG1. However, it remains unclear whether elevated foodspecific IgE levels are associated with the development of natural tolerance. We sought to better understand the role of food specific immunoglobulins in the development of food allergy and natural tolerance.

Methods: This cross-sectional study was approved by the Institutional Review Board (IRB) at Lurie Children’s Hospital, Chicago, IL. Informed consent was obtained from one legal guardian. Assent was obtained from children between ages 12 to 18 years old. Our study included subjects 6 months to 18 years old who had a allergist-diagnosed food allergy to egg, wheat, and/or peanut, or b) had previously diagnosed food allergy that was subsequently confirmed (natural tolerance), or c) were nonallergic. Food sensitization was evaluated by measurement of serum levels of food-specific IgA, IgE, and IgG4 to peanut, wheat, and egg, as well as total IgE levels, using the Phadia ImmunCAP system (Thermo Fisher Scientific, Waltham, MA).

Table 1. Patient Demographics

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Mean</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peanut allergy</td>
<td>0.1</td>
<td>4.4</td>
<td>0.1-12</td>
</tr>
<tr>
<td>Wheat allergy</td>
<td>0.1</td>
<td>4.4</td>
<td>0.1-12</td>
</tr>
<tr>
<td>Both peanut and wheat allergy</td>
<td>0.1</td>
<td>4.4</td>
<td>0.1-12</td>
</tr>
</tbody>
</table>

Results

Figure 1. Total IgE was elevated in subjects with food allergy compared to controls.

Figure 2. Food-specific IgG was undetectable in the serum of subjects with peanut allergy.

Figure 3. Peanut sIgE(A) and sIgG4(B) were higher in peanut allergic subjects compared to nonallergics and tolerant subjects.

Summary

- Subjects with food allergy have elevated levels of total serum IgE.
- Food-specific IgG was not detectable in most patients.
- Peanut allergic subjects have higher peanut sIgG4 compared to nonallergics and tolerant subjects.
- Subjects with peanut allergy, but not egg or wheat allergy, have elevated levels of egg- and wheat-specific IgE, even though they have been eating those foods.
- Subjects with egg allergy, but not peanut allergy, do not have elevated levels of peanut-specific IgE.
- Subjects with peanut allergy but not egg allergy have higher egg sIgG4 levels compared to nonallergic and egg allergic.

Conclusion

- IgE production is dysregulated in patients with peanut allergy, who are much less likely to outgrow and suggest that the mechanisms driving more persistent forms of food allergy may be distinct.
- Role of IgE may be better understood with local sampling in stool or intestinal mucosa.

References