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Impact of allergic reactions on food-specific IgE concentrations and skin test results

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Abstract

Background—Although there is concern that food allergic reactions may negatively affect the natural history of food allergy, the impact of reactions on food-specific IgE (sIgE) or skin prick tests is unknown.

Objective—To measure the effects of allergic reactions on SPT wheal size and sIgE concentrations to milk, egg and peanut.

Methods—Participants included 512 infants with likely milk or egg allergy enrolled in a multi-center observational study. Changes in sIgE and SPT to milk, egg, and peanut were measured before and after oral food challenge (OFC) or accidental exposure for 377 participants.

Results—Median age of the cohort at time of analysis was 8.5 years (67% male). There were no statistically significant changes in sIgE or SPT after positive OFC to milk, egg, or peanut (n=20-27 for each food). Change in sIgE and SPT was measured after 446 and 453 accidental exposure reactions, respectively. Median change in sIgE decreased by 0.33 kUA/L (p<.01) after milk and by 0.34 (p<.01) after egg reactions; but no other statistically significant changes in sIgE

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or SPT were observed for milk, egg, or peanut. Limiting analysis to only participants with diagnostic testing done within 6 months of an accidental exposure reaction, peanut SPT increased 1.75 mm ($p<.01$), but a significant increase was not noted when all participants with testing done within 12 months were considered.

Conclusions—The results suggest that reactions from OFCs and accidental exposure are not associated with increases in sensitization among children allergic to milk, egg or peanut.

Keywords

natural history; food allergy; IgE; skin prick test

INTRODUCTION

Food allergy is an important public health concern affecting up to 8% of children (1). Current management strategies require strict avoidance of causal foods and prompt treatment of allergic reactions, including treatment with injectable epinephrine for severe symptoms (2, 3). Strict dietary avoidance is difficult, and accidental or purposeful exposure to causal foods may occur (4). Accidental ingestions occur when an individual unknowingly or unintentionally ingests a food containing or contaminated with a food allergen. Purposeful (or non-accidental) ingestions occur when an individual knowingly ingests a causal food allergen either as the result of non-adherence to dietary instructions or during a diagnostic oral food challenge (OFC).

While the acute, potentially life-threatening risk of food allergen exposure is well described (3); the long-term impact of accidental or purposeful food allergen exposure on the long term prognosis of food allergy is unknown. We previously reported the annualized allergic reaction rate due to foods was 0.81 reactions per year among the current study population with >70% of participants reporting at least one unsupervised community exposure resulting in a food allergy episode (FAE) to a known food allergen over a 3-year period (4). In addition to FAEs occurring in the home or community, food allergic children are also exposed to food allergens when diagnostic OFCs are conducted for clinical or research purposes. The potential impact of these exposures on food-specific IgE (sIgE) concentrations and skin prick test (SPT) responses has not been previously reported. The consequences of these exposures, specifically the concern the reactions may reduce the chances of outgrowing a food allergy, is often questioned by patients, caregivers, and clinicians, and could result in deferral of OFCs (5). In previous investigations, seasonal environmental aeroallergen exposure has been associated with a rise in both serum allergen-specific IgE concentrations (6) and increase in skin prick sensitivity (7). It is unclear if a similar boosting effect occurs after ingestion of a food allergen. To our knowledge, prior studies have not examined changes in sIgE concentrations or SPT size before and after exposure to food allergens in a large pediatric cohort. Understanding the impact of accidental and/or purposeful food allergen exposure on these indices may inform patients, caregivers, and clinicians regarding the potential long-term impact of these exposures on the natural course of food allergy.

The aim of this investigation was to examine the change in sIgE concentration and SPT wheal size to milk, egg, and peanut before and following exposure to each respective food allergen. The study population consisted of 512 children with milk and/or egg allergy enrolled in a multicenter observational study aimed to examine immunologic, genetic, and environmental factors affecting the natural course of food allergy (8,9). Participants had OFCs when protocol-specified criteria were met and had blood drawn for serum IgE concentrations and SPTs performed at regularly scheduled visits. Caregivers reported FAEs in "real-time" after an exposure to a food allergen.

METHODS

Subjects

Participant characteristics and study enrollment procedures were previously reported (8,9). Briefly, this is an observational study of 512 infants in the Consortium for Food Allergy Research observational study (COFAR2) enrolled with likely egg or milk allergy who were not yet diagnosed with a likely peanut allergy, recruited at ages 3-15 months, and enrolled at 5 US sites (New York, NY, Baltimore, MD, Little Rock, AR, Denver, CO, Durham, NC). Infants fulfilled at least one of the following 2 criteria: 1) convincing allergic reaction to milk and/or egg with a positive prick skin test (SPT) to the trigger food(s), and/or 2) moderate to severe atopic dermatitis and a positive SPT to milk and/or egg. Infants were not enrolled if they had a confirmed or convincing allergy to peanut. A Data Safety Monitoring Board and local Institutional Review Boards approved study procedures, and written consents were obtained. Participants were scheduled for a clinical evaluation at 6-month intervals for 2 visits, and then yearly, with telephone contacts between each visit.

Inclusion in the current analysis required exposure to milk, egg or peanut during a first oral food challenge (OFC) to the individual food, whether or not a reaction occurred, or a first allergic reaction, termed a food allergy episode (FAE), after enrollment if tests for sensitization were available within a year before and following the exposure or challenge. The last enrollment to CoFAR2 was in March 2008; participants are still being followed, however, the database for this report was closed on February 12, 2015.

Oral Food Challenges (OFC)

Physician supervised oral food challenges were offered at clinician discretion and family preference guided by the protocol under the following circumstances: 1) there was no recent (past 6 months) reaction to the food, 2) Current test results (skin test/plasma IgE) indicated approximately a 50% or better chance of tolerance (egg, milk IgE < 2 kU_A/L, Peanut IgE < 5 kU_A/L if no past history, < 2 kU_A/L if positive history) and skin tests wheal < 10 mm. After 5 years in the study, OFCs were offered without requiring the aforementioned test results. The food challenges were generally performed without masking, and ingestion of a meal size amount (1 egg, 2 tablespoons peanut butter, 6-8 ounces of milk) without symptoms was considered "passing". The results in this report focus on the first OFC to milk, egg and/or peanut.

Food Allergic Episodes (FAE)

A structured questionnaire (4) was used to obtain details of allergic reactions related to unscheduled exposure to milk, egg or peanut. Participants were requested to contact the study site for any allergic reactions, at which time this information was recorded. Subjects were also queried about interval allergic reactions at each in-person or telephone encounter. Reaction severity was graded based upon Perry et al (10) as mild (skin and/or oral symptoms and/or upper respiratory symptoms but not all 3 organ systems); moderate (skin, oral and upper respiratory symptoms, or gastrointestinal symptoms); and severe (lower respiratory symptoms, cardiovascular symptoms or a combination of skin, oral, upper respiratory and gastrointestinal symptoms).

Skin Prick Tests (SPT) and Serum IgE (sIgE)

SPTs were performed using the GreerPick® (Lenoir, NC) with participants avoiding antihistamines for at least 5 half-lives of the specific agent. Tests were performed on the infant's back and at 15 minutes the wheal was outlined in pen and transferred by tape to paper. The size of the longest diameter and its longest perpendicular were averaged. The final SPT wheal size was determined after subtraction of the saline control. Tests were considered reliable if the wheal of the negative control (50% glycerin-saline) was 3 mm or smaller and wheal size of the histamine control was at least 3 mm larger than the wheal size of the negative control. The following extracts were used (Greer catalog number in parentheses, Lenoir, NC): cow milk (F293), chicken egg white (F272), and peanut (F171). The concentration of specific IgE antibody to egg, milk and peanut were measured from plasma at a single central laboratory using the Phadia ImmunoCAP® system (Uppsala, Sweden) reported in kUA/L.

Statistics

Summary statistics for demographics are presented whether or not a participant contributed to any of the analyses; differences in demographic characteristics for those participants in some analyses versus those not in any analyses were conducted using a chi-square test for categorical outcomes and a Wilcoxon rank sum test for continuous outcomes. For each of the OFC and FAE analyses of change in IgE or SPT, the Wilcoxon signed rank test is used to test whether the median change in the score differed from zero. The correlation between either the number of days between tests or the number of days after the test and the change in IgE or SPT was analyzed using Spearman's correlation. The association between levels of a baseline characteristic or event characteristic and the change in IgE or SPT score is tested with the Kruskal-Wallis test; baseline characteristics tested included age at FAE or OFC (grouped), race (grouped), ethnicity, clinical site, number of food allergies (milk/egg/peanut, grouped if necessary), and AD (grouped if necessary); event characteristics included severity of FAE symptoms. Characteristics were tested if a minimum number of participants were included in the levels of the characteristic; for some characteristics, if particular levels were sparse they were excluded or grouped (e.g., grouping atopic dermatitis as none to mild, and moderate to severe). Most factors could not be tested for an association with a positive or negative OFC results due to small numbers. Additionally, to explore a subgroup with larger changes in SPT/IgE, the association between being in the upper quartile of change

score and specified risk factors was analyzed using Fisher's exact test. The analyses focus on the first reported FAE for each of the three allergens or first OFC for each antigen; a participant could therefore contribute data to each of the FAE analyses (milk, egg, and/or peanut) and each of the OFC analyses. Subsequent FAEs and OFCs to the same food are not included in the analyses as restricting data to the first food-specific event removes carry-over effect from prior events in the same person. A large number of statistical tests were conducted for these analyses. Formal adjustments for multiplicity (e.g., Bonferroni or Benjamini-Hochberg) were not applied, as this was an exploratory analysis. Instead to help control for potentially spurious results, a p-value of <0.01 was used to define significance. An alternative exploratory analysis was performed by assuming that categorical changes in sIgE levels may be clinically relevant (for example if sIgE increased from <0.35 kUA/L to >1 kUA/L, 1-2 kUA/L decreases to <= 0.35 kUA/L, etc.) and these methods are shown in the Online Repository, Supplemental Analyses.

RESULTS

Demographic characteristics

Table E1 shows the demographic features of the children who underwent OFCs or experienced FAEs included in these analyses, compared to the remainder of the observational study cohort. The median months on study is 84.6 (IQR: 75.4 – 90.4) for those in the analyses included here compared to 70.0 (IQR: 53.8 – 84.2) months for those not in the analyses (p<0.01). The median IgE levels at enrollment for those undergoing OFCs was (kUA/L) milk- 0.9 (IQR: 0.2-4.2), egg- 1.4 (IQR: 0.2-5.6), and peanut-0.6 (IQR: 0.0-3.1), for those experiencing FAEs was milk-2.1 (IQR: 0.3-9.9), egg- 3.2 (0.7-11.5), and peanut-1.7 (0.2-9.8). For those in any of the OFC or FAE analyses, the median IgE levels at enrollment were (kUA/L) milk-1.4 (IQR: 0.2-7.3), egg- 2.9 (0.5-10.9), peanut-1.3 (0.1-8.1) and for those in the observational cohort but not included in any analysis, it was milk- 0.1 (IQR: 0.0-1.1), egg- 0.9 (0.1-3.6), and peanut-0.3 (0.0-2.2) (p<0.01 for each). Since OFC and FAE analyses are conducted separately for milk, egg, and peanut and separately for change in IgE and change in SPT, the actual distribution of participants in each analysis varies. At the time of data closure for this report, the overall observational study population had a median age of 8.5 years (IQR: 8.2 - 9.0). Among all participants with an OFC or FAE in the overall population, the median age (months) of a first OFC was milk 25.5 (IQR: 20.0 - 40.3), egg 35.3 (IQR: 26.0 - 51.0) and peanut 49.7 (IQR: 43.6 - 66.3), and the median age (months) of a first FAE was: milk 17.0 (IQR: 13.1 - 25.8), egg 22.2 (IQR: 15.7 - 38.2) and peanut 40.5 (IQR: 20.4 - 62.7).

Oral Food Challenges

Serum food-specific IgE—There were 229 OFCs among 157 participants meeting the criteria for the analysis of specific IgE: 82 milk (32% positive), 86 egg (26% positive) and 61 peanut (36% positive). The median time (days) that serum was obtained pre/post the OFC were: milk-70/278, egg- 97/250 and peanut-99/257. Considering positive OFCs only, for milk there was a median decrease of 0.10 kU_A/L (p=0.13) after the OFC, for egg a median decrease of 0.01 kU_A/L (p=0.69) and for peanut there was no change (p=0.60) (Figure 1a).

Skin prick tests—There were 225 OFCs among 153 participants meeting the criteria for the analysis of specific SPT results: 83 milk (33% positive), 83 egg (27% positive) and 59 peanut (34% positive). The median time (days) that skin testing was performed pre/post the OFC was milk- 69/272, egg- 92/250 and peanut- 99/262. Among positive OFCs, there were no statistically significant changes in skin test size (Figure 1b). Negative OFCs were associated with small significant decreases in skin test responses for milk and egg (Figure 1b and Table 1), possibly reflecting changes after time ingesting the food.

Food Allergy Episodes

Serum food-specific IgE—There were a total of 446 FAEs meeting analysis criteria among 319 participants: 205 milk, 156 egg and 85 peanut. The median time (days) that serum was obtained pre/post the FAE was: milk-116/95, egg-138/103 and peanut-177/131. There was a median decrease in milk specific IgE of 0.33 kU_A/L ($p<.01$), a decrease in egg specific IgE of 0.34 kU_A/L ($p<.01$) and an increase in peanut specific IgE of 0.13 kU_A/L ($p=0.029$, NS). Figure 2a shows the change in food specific IgE for the 3 foods. Considering demographic and clinical factors, including severity of reactions, there was no association with milk or peanut results. For egg, in grouping race as white versus non-white, there was a greater decrease among non-white (1.2 kU_A/L) than white (0.2 kU_A/L, $p<.01$).

Skin prick tests—There were 453 FAEs meeting the criteria for the analysis of specific SPT results among 325 participants: 207 FAEs to milk, 161 to egg and 85 to peanut. The median time (days) that skin testing was performed pre/post the FAE was: milk-108/95, egg-138/101 and peanut-166/132. Figure 2b shows the SPT results to all 3 foods. There was no change in median SPT wheal size for milk (0.0 mm; $p=0.55$, NS) and a decrease for egg (1.0 mm; $p=0.09$, NS) and increase for peanut (1.5 mm, $p=0.02$, NS). Considering the demographic and clinical factors described previously, none were associated with the results.

Results limiting window of time between food exposure and testing—The time of testing of SPT or specific IgE testing was dictated by the timing of annual study visits and not aligned with OFCs or FAEs. Therefore, there was a wide range of times between events and testing, as noted above. It could be hypothesized that changes due to exposure may be more evident if tests were done proximate to reactions. We therefore limited analyses to events with samples obtained within 6 months or 1 month of an FAE or within 6 months of an OFC. Regarding data within 6 months of a positive OFC, there were not more than 7 OFCs for outcomes except change in SPT after positive milk OFC, which did not have a statistically significant difference (data not shown). Data for FAEs are shown in Table 2. The data are limited by decreasing numbers of participants when narrower times are evaluated. One statistically significant outcome was noted in these restricted time periods: peanut SPT increased 1.75 mm ($p<.01$) when evaluations were limited to testing within 6 months of an FAE. These results were in the same direction (increase) as results obtained in the 1 year time frame. In an additional analysis to explore the association of change scores with time, there was no strong correlation (Spearman correlation coefficient less than −0.5 or greater than 0.5) between the changes in IgE or SPT and either the number of days

between each participant's before and after tests or the number of days after the test, within any of the egg, milk, or peanut analyses.

Results of additional exploratory analyses—Additional analyses were conducted to specifically assess those children with greater increases in IgE or SPT, focusing on the upper quartile of change for association with specified risk factors, to determine if this group had identifiable risk factors. For FAE results, no baseline clinical or demographic characteristic tested was associated with results in the upper quartile of response for any of the foods. There were too few participants in the OFC studies to perform this analysis. The additional, alternative analysis using categorical changes in IgE levels support the main conclusions of the paper, as reviewed in the Online Repository Supplemental Analyses.

DISCUSSION

The difficulties of elimination diets in the management of food allergy are well established, with frequent accidental reactions occurring as a result. For example, we previously reported in the full CoFAR observational study cohort an annualized rate of 0.81 accidental reactions per year (4). However, the prognostic implications, if any, of such exposures is unknown. Similarly, food allergic children are exposed to known food allergens during diagnostic OFCs, and the long-term impact of these exposures has not been previously established. The question of specific interest in the current study was whether such intermittent exposures negatively influence the trajectory of the allergy by intensifying or prolonging allergic sensitization. For this reason, and because some of the children entered this study without previously documented oral exposure, we focused only on symptomatic exposures, FAEs or failed OFCs, in participants who were thus known to be allergic. We report here that there were no statistically significant changes in sIgE or SPT following positive OFCs to milk, egg or peanut. IgE levels and skin test sizes reflect risk of current allergy.(1-3) The overall lack of any significant change in skin test or IgE level from OFC induced reactions suggests that there is no change in the reaction risk following the exposure compared to before the exposure. The several significant median changes from FAEs for egg and milk were small decreases, which should not correlate with any increased risk of reactions. The median peanut FAE related increase of 0.13 kUA/L and SPT 1.5 mm is unlikely to reflect significant changes in risk.

We hypothesized that there could be factors, such as a more severe reaction, that could account for persons having a greater increase in sensitization parameters post-exposure. However, when exploratory analysis was performed to determine if there were factors associated with those having the highest quartile of change after FAE, none were identified.

Some sensitization parameters showed statistically significant increases. In the case of peanut, median serum-specific IgEs and SPTs increased by 1.3 kU_A/L ($p=0.02$ NS) and 1.75 mm ($p<0.01$), respectively, in participants who were assessed within six months of the symptomatic FAE. However, the decrease in observed difference and lack of a detectable change at the 0.01 level in these parameters when including participants measured up to one year after the FAE suggests that this small upward deflection is ultimately inconsequential. In contrast to peanut, egg and milk sensitization parameters showed small, post exposure

decreases. The reason for this difference in direction of change is unknown, and could be related to adjuvant or other effects, but ultimately all changes in sensitization were small and presumably clinically insignificant or overall not elevated up to one year following exposure.

Because this cohort was not specifically designed a priori to answer the research question at hand, the protocol did not standardize the collection of skin or serum outcome variables in relation to planned or accidental exposures. Instead, these parameters were measured at fixed intervals related to time of study enrollment. As a result, the intervals between exposures and the measurements of sensitization were not uniform among participants and the data are somewhat limited by the necessarily post hoc approach to the analysis. It remains possible that the observed heterogeneity with respect to timing of measurements could lead to an imprecision of the effects of exposures on the outcome variables. However, it can be reasonably concluded that (1) the variation occurs randomly; and, (2) when viewed across the study population, the average long-term effects are minimal. Importantly, the severity of FAE reaction did not associate with increases in the sIgE or SPT. We are not aware of any similar analyses of the longitudinal effects of unplanned accidental exposures among a cohort of children prospectively enrolled in an IRB-approved observational protocol in which allergen avoidance was advised. This observational study precluded the possibility of a matched control group that was followed without a food challenge that had passed a food challenge but was required not to ingest the food, or controls without any accidental exposure. Such a group cannot be identified from this cohort because there would be clinical differences between groups selected for OFCs, it would not be practical to prescribe avoidance after a subject passed an OFC in the context of this study, and it is always possible that accidental exposures occurred without obvious reactions, specifically in children already having become tolerant, which would invalidate comparisons with children who reacted. Therefore, we focused our analysis using participants as their own controls and did not observe meaningful increases in IgE or skin tests, the primary concern in clinical situations. As described in the Online Repository Supplemental Analyses, the trajectory of sIgE levels in the children having reactions paralleled the cohort as a whole. Nonetheless, having matched controls or a controlled trial of randomized exposures would have allowed analysis of any potential difference in natural course; such a study may also need to investigate any effects of pollen exposure on peanut tests.

Most data about the longitudinal effects of allergen exposures are derived from natural history studies of real-world populations attending clinics (11-19). In general, such studies are often performed at academic centers using retrospective chart review methods and tend to report on the relationship of IgE levels to allergen exposures in the context of planned OFCs (i.e. in children expected to be improving), rather than FAEs. Although these data carry with them important sources of bias including attrition and selection, and most participants are not challenged at study entry, they have nonetheless demonstrated that tolerance to foods is associated with falling IgE levels, a fact which is now well accepted (20). This finding has been replicated in an unselected, prospectively enrolled population-based cohort in which participants underwent baseline and follow-up OFCs regardless of IgE level (21). While the persistence of food allergies (i.e., failing an OFC) was associated with higher allergen-specific IgE levels in essentially all of these studies, there is no

evidence from the studies involving serial OFCs (14, 16-19) that the levels were boosted by a failed challenge. It is important to note that prior to the establishment of predictive thresholds, there are subjects in some of these studies that failed annual OFCs for as many as ten years before resolving (19). Our study, in which failed OFCs resulted in clinically insignificant changes in IgE and SPT, further support the conclusion that such exposures do not worsen allergic sensitization among young children with egg, milk, and/or peanut allergy. We emphasize that we have evaluated the impact of single event oral exposures, in contrast to more persistent exposures that are known to increase specific IgE levels, for example during the pollen season or during oral immunotherapy. (6,7,22)”

The strengths of this study include its sampling of a large number of real-world clinical patients at multiple U.S. sites, years of longitudinal follow-up, and a uniform and protocolized approach to the collection of immunologic and extensive FAE data through a 30-item questionnaire (4). These factors contribute to the validity of the study by facilitating comprehensive ascertainment of unplanned events and their sequelae.

We believe that the data presented here support the notion that occasional oral food allergen exposures, whether through accidents or planned food challenges, do not lead to enhanced sensitization that would delay resolution or otherwise worsen the long-term prognosis. If confirmed by other well-designed studies, these findings should provide a measure of comfort to both physicians and families as they deal with the aftermath of allergic reactions following food challenges or accidental exposures.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

AD	atopic dermatitis
CoFAR	Consortium of Food Allergy Research
FAE	food allergy episode
OFC	oral food challenge
sIgE	food-specific serum IgE

SPT	skin prick test
IQR	interquartile range
NS	not statistically significant

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What is already known about this topic?

Exposure to allergens, for example in the pollen seasons or during immunotherapy, can result in increases in specific IgE, but it is not known whether one-time exposures to food allergen ingestion meaningfully alter IgE levels.

What does this article add to our knowledge?

Accidental or food challenge exposure to milk, egg or peanut that resulted in allergic reactions in children were not associated with significant increases in skin test size or allergen-specific IgE levels.

How does this study impact current management guidelines?

The results suggest that oral food challenges should not be deferred due to concerns that reactions could affect prognosis.

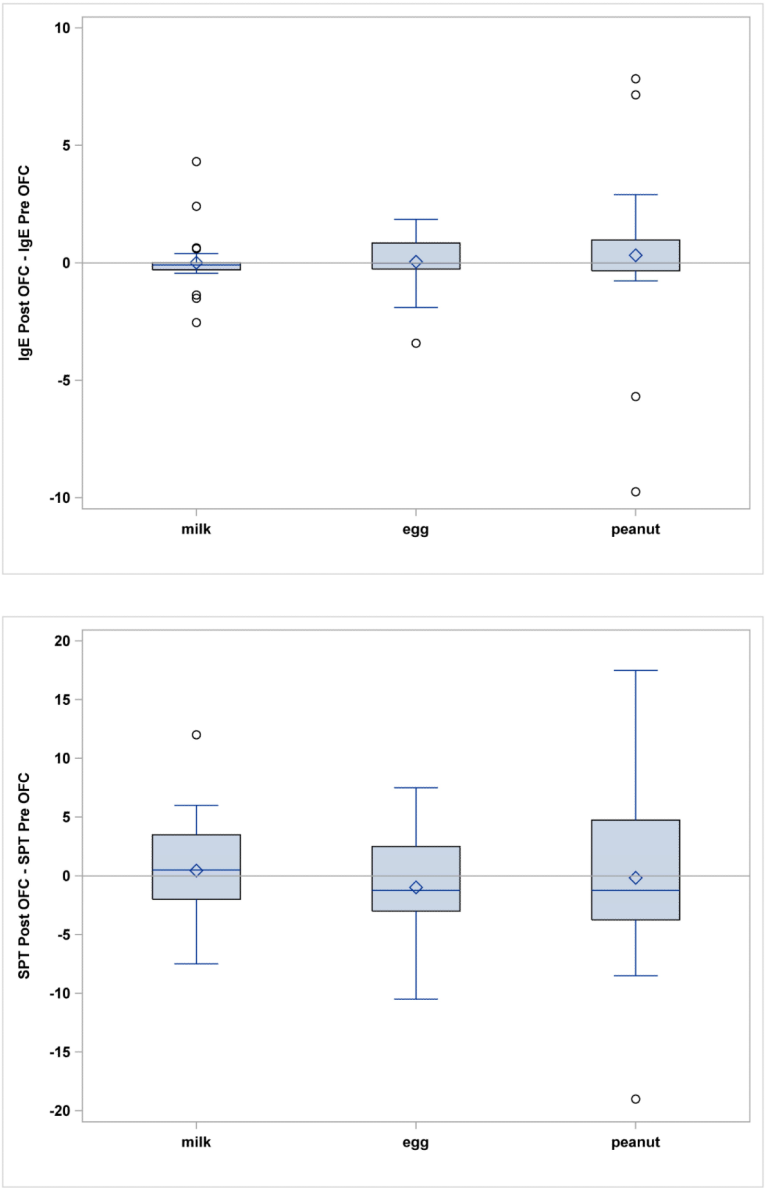

Figure 1.

Median change in sIgE concentrations and SPT wheal size following reactions during OFCs. Panel 1a depicts change in sIgE. Median milk-specific IgE decreased by 0.10 kU_A/L (p=0.13), egg-specific IgE decreased by 0.01 kU_A/L (p=0.69) and no change for peanut (p=0.60). Panel 1b depicts change in SPT. No changes in SPT size were observed. The box encompasses quartiles 1-3, the line across the box marks the median and the diamond marks the mean. Circles are values more extreme than 1.5 times outside the interquartile range. P values <0.01 were considered statistically significant.

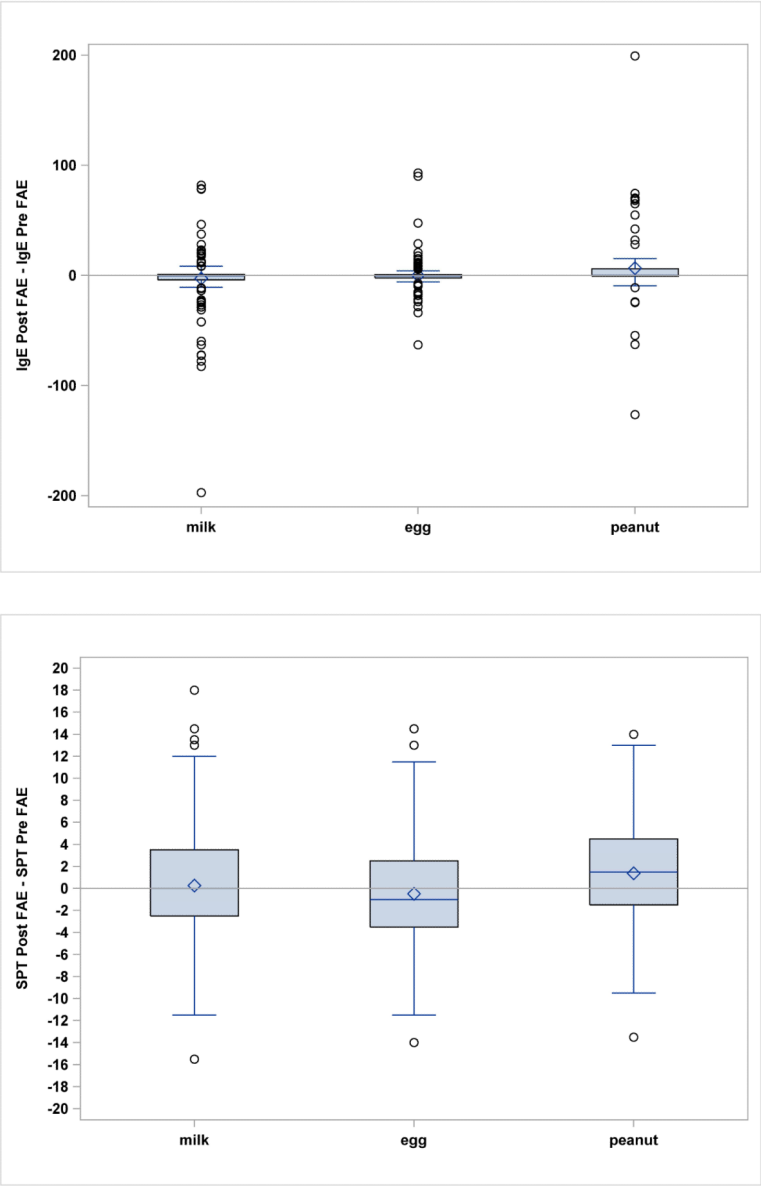

Figure 2.

Median change in sIgE concentration and SPT wheal size following FAEs. Panel 2a depicts change in sIgE. Median milk-specific IgE decreased by 0.33 kU_A/L ($p<.01$), egg-specific IgE decreased by 0.34 kU_A/L ($p<0.01$) and peanut-specific IgE increased by 0.13 kU_A/L ($p=0.03$). Panel 2b depicts change in SPT. No change in SPT size was observed for milk. Egg SPT decreased by 1.0 mm ($p=0.09$) and peanut SPT increased by 1.5 mm ($p=0.02$). The box encompasses quartiles 1-3, the line across the box marks the median and the diamond marks the mean. Circles are values more extreme than 1.5 times outside the interquartile range. P values <0.01 were considered statistically significant.

Table 1

Food-specific IgE and SPT results for positive and negative OFCs.

Food/Test	Oral food challenge result	N	Median value pre/post	Median change	p-value
Milk IgE	Positive Negative	26 56	0.66/0.42 kU_A/L 0.34/0.27 kU_A/L	−0.10 kU_A/L −0.00 kU_A/L	0.13 0.11
Milk SPT	Positive Negative	27 56	5.00/6.00 mm 3.00/0.00 mm	0.50 mm −2.50 mm	0.80 **P<.01**
Egg IgE	Positive Negative	22 64	0.70/1.30 kU_A/L 0.25/0.21 kU_A/L	−.01 kU_A/L −.02 kU_A/L	0.69 0.32
Egg SPT	Positive Negative	22 61	6.50/6.50 mm 2.50/0.00 mm	−1.25 mm −0.50 mm	0.37 **P<.01**
Peanut IgE	Positive Negative	22 39	1.20/2.00 kU_A/L 0.14/0.12 kU_A/L	−0.00 kU_A/L −0.01 kU_A/L	0.60 0.54
Peanut SPT	Positive Negative	20 39	9.50/9.75 mm 0.00/0.00 mm	−1.25 mm 0.00 mm	0.96 0.14

Table 2

Results limiting window of time between FAE and post-exposure testing to 12, 6, or 1 months

Food/Test type	Time from event	N	Median value pre/post	Median change	p-value
Milk/IgE	Within 12 months	205	5.21/4.14 kU_A/L	−0.33 kU_A/L	**−p<.01**
	Within 6 months	174	5.00/3.86 kU_A/L	−0.33 kU_A/L	0.022
	Within 1 month	46	2.31/2.14 kU_A/L	−0.22 kU_A/L	0.215
Milk/SPT	Within 12 months	207	9.00/10.00 mm	0.00 mm	0.547
	Within 6 months	182	8.50/9.50 mm	0.00 mm	0.432
	Within 1 month	44	8.00/9.50 mm	0.00 mm	0.953
Egg/IgE	Within 12 months	156	4.18/3.31 kU_A/L	−0.34 kU_A/L	**p<.01**
	Within 6 months	122	3.46/3.29 kU_A/L	−0.32 kU_A/L	0.064
	Within 1 month	31	5.97/3.72 kU_A/L	−0.33 kU_A/L	0.408
Egg/SPT	Within 12 months	161	8.50/8.50 mm	−1.00 mm	0.092
	Within 6 months	129	8.50/9.00 mm	−1.00 mm	0.120
	Within 1 month	34	7.25/10.50 mm	0.25 mm	0.545
Peanut/IgE	Within 12 months	85	7.44/8.33 kU_A/L	0.13 kU_A/L	0.029
	Within 6 months	57	8.45/9.29 kU_A/L	1.3 kU_A/L	0.018
	Within 1 month	7	2.29/5.60 kU_A/L	1.3 kU_A/L	--
Peanut/SPT	Within 12 months	85	10.00/10.00 mm	1.50 mm	0.022
	Within 6 months	54	10.00/10.50 mm	1.75 mm	**p<.01**
	Within 1 month	8	10.25/17.25 mm	4.75 mm	0.047