Allergic Reactions to Foods in Preschool-Aged Children in a Prospective Observational Food Allergy Study


**PURPOSE OF THE STUDY.** To determine the frequency and circumstances of allergic reactions to common food allergens in a multicenter, prospective study of preschool-aged children.

**STUDY POPULATION.** The cohort examined was already participating in an observational study to monitor for development of peanut allergy in patients with history of milk/egg allergy. There were 512 infants enrolled between the ages of 3 and 15 months from 5 US sites.

**METHODS.** In a prospective, 5-site observational study, subjects were scheduled for a clinical evaluation at 6-month intervals for 2 visits, then yearly with telephone contacts between each visit. Baseline immunoglobulin E to specific allergens was also obtained. Written and verbal specific food allergen avoidance instructions, along with treatment plans with prescriptions for self-injectable epinephrine were provided. A 36-item questionnaire obtained details about the occurrence of an immunoglobulin E-mediated reaction, including symptoms and time of occurrence, trigger, route of exposure (accidental versus purposeful), and response to reaction.

**RESULTS.** Over the median follow-up of 36 months, annualized reaction rate was 0.81 per year for all foods (367/512 subjects reporting 1171 reactions) with 56% reporting >1 reaction. Most were triggered by milk (42.0%), egg (21.0%), and peanut (7.9%). Most (64.9%) accidental allergic reactions were attributed to lack of vigilance (eg, label-checking errors and unintentional ingestion). Additional errors included cross-contact in meal preparation and food not provided by actual caregivers. Approximately 11% of reactions were attributed to nonaccidental exposure. Of the 11.4% of reactions that were severe, only 29.0% of them were treated with epinephrine because the caregiver did not recognize the severity, the epinephrine was unavailable, or the caregiver was afraid to administer it.

**CONCLUSIONS.** Because of the high frequency of reactions in preschool-aged subjects, there needs to be an emphasis on improving education in the parent and other caregivers about exposure prevention and anticipatory guidance. The education needs to include indications for epinephrine use and proper technique, as well as potential complications.

**REVIEWER COMMENTS.** This novel prospective, observational study used a large cohort of preschool-aged children. The number of purposeful exposures and the lack of vigilance, despite initial anticipatory guidance, is remarkable. This article emphasizes the importance of providing patients and all caregivers with anticipatory guidance at every clinic visit and reviewing their knowledge of the potential reaction on exposure. It is very important to emphasize the need for supervision, label reading, possible dangers of unsupervised allergen reintroduction, and the symptoms that warrant treatment with epinephrine. The study is limited by parental bias in reporting reaction and circumstances, as well as recall bias.

**Oral Immunotherapy for Treatment of Egg Allergy in Children**


**PURPOSE OF THE STUDY.** To determine that oral immunotherapy (OIT) to egg is safe and effective to desensitize patients and induce sustained unresponsiveness.
STUDY POPULATION. A double-blind, randomized placebo-controlled study of 55 children, 5 to 11 years of age, sensitive to egg, with 40 receiving OIT and 15 placebo.

METHODS. Initial dose escalation and buildup, maintenance phases up to 2 g of egg protein (one-third egg). This was followed by an oral food challenge with egg white powder at 10 months and 22 months. Children who successfully passed the challenge at 22 months discontinued OIT and avoided egg consumption for 4 to 6 weeks. At 24 months, these children had oral food challenge with egg powder and a cooked egg to test for unresponsiveness.

RESULTS. After 10 months of therapy, none of the children who received placebo and 55% of those who received OIT passed an oral food challenge of up to 5 g of egg protein and were considered desensitized. At 22 months, 75% of children in the OIT group were desensitized and tolerated up to 10 g of egg protein. In the OIT group, 28% passed the oral food challenge at 24 months and were considered to have sustained unresponsiveness. At 30 to 36 months, all children who had passed the oral food challenge at 24 months were consuming egg without restrictions.

CONCLUSIONS. This study shows that OIT can desensitize a high proportion of children with egg allergy and induce sustained unresponsiveness.

REVIEWER COMMENTS. This landmark study shows that desensitization, an increased threshold while on daily treatment, to egg protein can be achieved in most patients with a 1% rate of more than mild reactions during OIT. Having 28% achieve sustained unresponsiveness off daily treatment is encouraging, but more studies are needed to determine if this observation reflects a treatment “cure” or natural course of the allergy. Overall, this study provides a step forward to help patients with significant egg sensitivity to not only ensure safety but also allow ingestion of egg protein.


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Sublingual Immunotherapy for Peanut Allergy: A Randomized, Double-Blind, Placebo-Controlled Multicenter Trial

PURPOSE OF THE STUDY. To determine the safety and efficacy of sublingual immunotherapy (SLIT) for inducing desensitization in subjects with peanut allergy.

STUDY POPULATION. The study population consisted of 40 subjects (ages 12–37 years) from 5 US sites with peanut allergy defined by clinical history or physician diagnosis, positive skin-prick test or peanut-specific immunoglobulin E (Pn-IgE; ≥0.35 kU/L), and a positive double-blind, placebo-controlled oral food challenge (OF C) to ≤2 g of peanut powder. Patients with a history of severe anaphylaxis to peanut were excluded.

METHODS. Subjects were randomly assigned 1:1 to peanut (Pn) or placebo (Pb) SLIT groups. Subjects started with an initial daily SLIT dose (peanut = 0.000165 μg), with dose escalation every 2 weeks up to a maximum dose of 1386 μg. A 5-g OFC to peanut powder (2.5 g of peanut protein) was conducted at week 44. Subjects in the Pb-SLIT group crossed over to high-dose-plant peanut SLIT (3696-μg target dose) and received a 5-g OFC after 44 weeks, whereas Pn-SLIT subjects continued dosing until a 10-g OFC at 68 weeks. Responders were defined as those able to consume 5 g of peanut powder or a 10-fold increase over baseline OFC. Total IgE levels, Pn-IgE, Pn-immunoglobulin G4 (IgG4), and basophil activation were monitored at baseline and during the study.

RESULTS. Subjects in the Pn-SLIT group showed a significantly higher response at 44 weeks compared with those in the Pb-SLIT group (70% vs 15%, respectively; P < .001), with a successfully consumed dose (SCD) that was higher in the Pn-SLIT group compared with the Pn-SLIT group (371 vs 21 mg, respectively; P = .01). After 68 weeks of Pn-SLIT, the median SCD further increased to 996 mg (P = .05). The median SCD in the week 44 crossover OFC was higher than baseline (603 vs 71 mg; P = .02). From baseline to week 44, 99.4% of the placebo group was symptom-free compared with 59.9% of the Pn-SLIT group. Pn-IgE and Pn-IgG4 in the Pn-SLIT group increased between baseline and week 44 only (P = .035). No statistical difference in Pn-IgE or Pn-IgG4 was found at week 44 between Pb-SLIT and Pn-SLIT, Pn-SLIT responders and nonresponders, or the crossover high-dose group and the Pn-SLIT group. Basophil activation was significantly lower in the Pn-SLIT group compared with the Pb-SLIT group. The Pn-SLIT responders showed a reduction in skin-prick test compared with nonresponders at week 44 (P = .03).

CONCLUSIONS. This study reveals a significant effect of Pn-SLIT in inducing desensitization. During 10,885 doses of Pn-SLIT, 95.3% of subjects were symptom-free at week 44 when oropharyngeal symptoms were excluded.

REVIEWER COMMENTS. This was the first multicenter, randomized, placebo-controlled trial to examine SLIT in peanut-allergic subjects. This trial demonstrates a significant degree of desensitization in peanut-allergic subjects by using a treatment with a low side-effect profile. Whereas there are limitations highlighted in this study, this is an important development in therapy for peanut allergies that necessitates further investigation.
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