**RESULTS.** Among a total of 150 OFCs, most of which were to milk (n = 39), peanut (n = 37), and egg (n = 29), there were 40 positive test results (27% of all challenges) in 33 patients. Reactions were mild-to-moderate in 92% of the positive challenges. Cutaneous reactions occurred in 68% of the positive challenges, followed by gastrointestinal tract reactions (45%) and upper respiratory tract reactions (38%), excluding laryngeal symptoms. No patient had cardiovascular involvement, received epinephrine, or required hospitalization. Interventions included observation or antihistamine only for 92% of the positive challenges. Food-specific IgE values did not correlate with reaction severity. Of the 23 OFCs to milk, egg, and peanut without a history of clinical reactions, 8 were positive. For negative challenges, median prechallenge food-specific IgE levels approached previously published positive. For negative challenges, median prechallenge peanut without a history of clinical reactions, 8 were with reaction severity. Of the 23 OFCs to milk, egg, and peanut without a history of clinical reactions, 8 were positive. For negative challenges, median prechallenge food-specific IgE levels approached previously published negative predictive values for these foods (1.22 kU/L for milk, 0.96 kU/L for peanut, and 0.65 kU/L for egg). Negative challenge results for patients allowed the introduction of 19 different foods into the diets of 88 patients.

**CONCLUSIONS.** The authors concluded that OFCs are a safe procedure in the office setting for patients selected on the basis of food-specific IgE levels that approach negative predictive values and a lack of adverse reactions within the previous year.

**REVIEWER COMMENTS.** This nice report suggests that open OFCs performed by experienced practitioners in a clinic setting on carefully selected patients can be of significant benefit for patients who are tolerant to a food to avoid unnecessarily restrictive diets. Keeping in mind that the authors detected positive challenges in 4 patients with an undetectable food-specific IgE level and that there was a lack of association between the food-specific IgE level and severity of a reaction, prechallenge skin-prick tests and careful review of the clinical history should be used. Every challenge should be approached with appropriate precautions (emergency medications and equipment readily available) to treat potentially severe reactions.

**Specific Oral Tolerance Induction in Food Allergy in Children: Efficacy and Clinical Patterns of Reaction**


**PURPOSE OF THE STUDY.** To evaluate the efficacy of oral tolerance induction as a treatment for cow’s milk and egg allergies.

**STUDY POPULATION.** Forty-seven children aged 0.6 to 12.9 years with positive double-blind, placebo-controlled food challenges to milk or hen’s egg were included in this German study. Children with severe eczema were excluded.

**METHODS.** Subjects were randomly assigned to specific oral tolerance induction or continued avoidance. Treatment involved home escalation over at least 67 days from a dose of 1 drop of cow’s milk to 250 mL or from 5 mg of lyophilized hen egg powder to 3500 mg. Subjects continued home dosing for a median of 21 months total, after which time they underwent a secondary period of avoidance for 2 months followed by a food challenge.

**RESULTS.** At follow-up challenge, 9 (36%) of 25 children in the specific-oral-tolerance-induction group showed permanent tolerance, 3 (12%) of 25 were tolerant with regular intake, 4 (16%) of 25 were partial responders, and 9 (36%) of 25 did not complete the treatment because of adverse effects. In the control group, 7 (35%) of 20 children were tolerant at the study end. Allergen-specific IgE levels decreased in children who developed tolerance both in the control (P < .05) and treatment (P < .001) groups.

**CONCLUSIONS.** Specific oral tolerance induction may be a valid treatment option for patients with persistent food allergy. However, only a minority of patients had evidence of persistent tolerance once treatment was stopped, with some unable to tolerate the therapy and others seeming to be only transiently desensitized.

**REVIEWER COMMENTS.** Allergen-specific immunotherapy with injected extracts has proven too dangerous to be a viable treatment method for food allergy. Sublingual or oral immunotherapy, as described here, is a promising alternative to strict avoidance. Although one third of the patients in this study had to withdraw because of adverse effects, the remaining patients were able to incorporate the allergen into their diet at some level. This treatment modality is highly promising, but it is still experimental, carries the potential for significant risk, and requires close monitoring by experienced physicians. Several studies of oral and sublingual immuno-
Specific Oral Tolerance Induction in Children With Very Severe Cow’s Milk-Induced Reactions

PURPOSE OF THE STUDY. To evaluate the safety and efficacy of specific oral tolerance induction for children with severe cow’s milk protein (CMP) allergy.

STUDY POPULATION. The study included 97 children (aged 5 to 17 years) with a history of severe allergic reactions and CMP-specific immunoglobulin E (IgE) levels of >85 kU/L.

METHODS. All subjects underwent a double-blind, placebo-controlled food challenge (DBPCFC) starting with very low amounts of diluted milk. Children were considered eligible for random assignment only if they had symptoms during the DBPCFC to the lowest doses (0.8 mL of whole milk). Sixty had positive test results and were randomly assigned to 1 of 2 groups: group A started the specific-oral-tolerance-induction protocol immediately after the DBPCFC; and group B maintained a milk-free diet for 1 year and then underwent another DBPCFC. CMP-specific IgE levels were obtained at enrollment and at 6 and 12 months. Subjects in group A were monitored as inpatients for 10 days during rapid, daily increases in milk dosage and then discharged from the hospital with instructions for increasing milk ingestion to a final goal of 150 mL per day. Once on 150 mL, subjects were instructed to add dairy products to their diet.

RESULTS. After 1 year, 11 (36%) of 30 children in group A were tolerant to the highest dose of 150 mL of cow’s milk per day with some ingesting additional dairy products, thus allowing them an unrestricted diet. Sixteen (54%) could take limited amounts of milk (5–150 mL), and 3 (10%) were not able to complete the protocol because of persistent respiratory and abdominal complaints. CMP-specific IgE levels measured in group A at 6 and 12 months showed a significant decrease in 15 of 30 subjects. In subjects in group B, DBPCFC results were positive with only minimal amounts of milk in all 30 cases, and only 2 subjects showed a decrease in specific IgE levels. Clinical differences between the groups were significant (P < .001). Adverse reactions were common among the subjects in group A, with multiple subjects requiring treatment throughout the protocol. It is interesting to note that 20% of the subjects in group B had adverse reactions after accidental exposure to CMP.

CONCLUSIONS. Specific oral tolerance induction is effective in a significant number of patients with severe cow’s milk allergy.

REVIEWER COMMENTS. Oral desensitization is a novel form of immunotherapy that is under investigation for food allergy, with benefits noted in several clinical studies. Unlike previous studies, this study addressed oral desensitization in children with very severe cow’s milk allergy. The authors noted their success among the subjects studied but were also quick to point out the number of adverse events that occurred when using their protocol. These results are encouraging for patients who suffer from food allergy but highlight the need for additional studies before implementation in clinical practice and the need for close monitoring in highly controlled settings.

ANAPHYLAXIS

Platelet-Activating Factor, PAF Acetylhydrolase, and Severe Anaphylaxis

PURPOSE OF THE STUDY. To characterize the roles of platelet-activating factor (PAF) and PAF acetylhydrolase, the enzyme that inactivates PAF, in humans.

STUDY POPULATION. The population was a variety of pediatric and adult patients with different levels of allergic disease along with nonallergic controls.

METHODS. Serum PAF levels and activity of PAF acetylhydrolase were measured in 41 patients with anaphylaxis and in 23 control patients. Serum PAF acetylhydrolase activity was also measured in 9 patients with fatal anaphylaxis and compared with that in 26 nonallergic pediatric control patients, 49 nonallergic adult control patients, 63 children with mild peanut allergy, 24 patients with nonfatal anaphylaxis, 10 children who died of nonanaphylactic causes, 15 children with life-threatening asthma, and 19 children with non–life-threatening asthma.

RESULTS. Mean serum PAF levels were significantly higher in patients with anaphylaxis than in patients in the control groups and were correlated with the severity of anaphylaxis. The proportion of subjects with elevated
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