CONCLUSIONS. Placing a child on EHCF accelerates tolerance acquisition in children with cow’s milk allergy compared with other formula choices and is further improved with the addition of LGG.

REVIEWER COMMENTS. The results shown in this study with EHCF resulting in a greater rate of tolerance acquisition is likely due to the immunomodulatory effect induced by hydrolyzed casein peptides, as suggested from previous animal studies. This benefit will have to be factored in when specifically considering starting patients on EHCF versus AAF because some patients will react even to EHCF. The difference in the rate of tolerance acquisition between EHCF and AAF may be that those requiring AAF have a more severe form of milk sensitivity, thus requiring them to be on AAF initially.

CONCLUSIONS. This study is the first to show sustained unresponsiveness after peanut OIT noted in ~50% of subjects treated for up to 5 years, results that persisted after OIT. Smaller SPT results and lower peanut-specific IgE levels strongly correlated with success of treatment.

REVIEWER COMMENTS. Sustained unresponsiveness in peanut OIT is a vital step in the treatment of peanut food allergies. This advancement in OIT is associated with direct benefit that likely requires ongoing antigen exposure for persistence. Further study in larger populations is needed to advance OIT as a viable treatment option for widespread use.

Sustained Unresponsiveness to Peanut in Subjects Who Have Completed Peanut Oral Immunotherapy


PURPOSE OF THE STUDY. The goal of this study was to determine if long-term treatment with oral immunotherapy (OIT) will result in sustained unresponsiveness to peanut.

STUDY POPULATION. The study enrolled 39 children, ages 1 to 16 years, with peanut allergy defined as a clinical history of a reaction to peanut within 60 minutes of ingestion, a positive peanut skin prick test (SPT) result ≥3 mm, and peanut-specific immunoglobulin (Ig)E ≥15 kU/L or with a positive SPT result and peanut IgE ≥7 kU/L and a clinical reaction within the previous 6 months. Subjects with poorly controlled or severe asthma and those with a history of severe anaphylaxis were excluded.

METHODS. Daily OIT was administered by using a standard protocol with initial dose escalation, build-up every 2 weeks to 4000 mg, and daily maintenance dosing for up to 5 years of therapy. Blinded oral food challenges (OFC) to 5000 mg of peanut were performed during and at the end of the study, including after 4 weeks of OIT cessation to assess sustained unresponsiveness. Peanut SPT, IgE testing, and immunologic assays were conducted throughout the study. A telephone survey was conducted at the end of the study to assess peanut consumption and symptoms noted.

RESULTS. Twenty-four of the 39 subjects completed the protocol. Six subjects withdrew due to allergic adverse effects, and 9 withdrew for other reasons. Twelve subjects demonstrated sustained unresponsiveness after the final OFC and were deemed treatment successes (TS) and were instructed to add peanut ad libitum to their diet; those not passing the final OFC were considered treatment failures (TF) and were instructed to continue dietary avoidance of peanuts. At baseline and final OFC, TS had smaller SPT results (P < .01) and lower peanut-specific IgE (P < .01), Ara h 1 (P < .05), and Ara h 2 (P < .01) levels plus a reduced peanut-specific IgE/total IgE ratio (P < .001) compared with TF. Peanut IgG4 levels did not differ between the 2 groups. Survey results showed that none of the TS reported allergic reactions to peanut compared with 14% of TF. TS consumed a median of 555 mg/d (0–4000 mg/d) of peanut 3 days per week (0–7 days/week).

Assessing the Efficacy of Oral Immunotherapy for the Desensitisation of Peanut Allergy in Children (STOP II): A Phase 2 Randomised Controlled Trial


PURPOSE OF THE STUDY. The goal of this study was to establish the efficacy of oral immunotherapy (OIT) for the desensitization of children with peanut allergy.

STUDY POPULATION. Children ages 7 to 16 years with an immediate peanut hypersensitivity reaction and a positive result on skin prick test and double-blind, placebo-controlled food challenge (DBPCFC) to peanut were recruited from allergy clinics and national patient support groups.

METHODS. In phase 1 of this unmasked, randomized, placebo-controlled trial, children in the active OIT group received 2 to 800 mg/d of peanut protein, and those in the control group continued to avoid peanut. The primary outcome was desensitization, defined as passing a DBPCFC to 1400 mg of peanut protein after 6 months. During phase 2, control participants remaining allergic to peanut received OIT and had a repeat DBPCFC.
RESULTS. Desensitization occurred in 24 (62%) of the 39 children on active OIT (95% confidence interval: 45–78) and in none of the 46 control children (95% confidence interval: 0–9; \( P < 0.001 \)). Of the active OIT group, 84% (95% confidence interval: 70–93) tolerated at least 800 mg of peanut protein (~5 peanuts), with a median increase in peanut threshold after OIT of 1345 mg (range: 45–1400 mg; \( P < 0.001 \)). Similar results were seen in phase 2. Oral pruritus and gastrointestinal symptoms were the most common adverse effects. Wheezing occurred after 0.41% of doses and in 21 children, 1 of whom received intramuscular epinephrine; laryngeal edema occurred after 0.01% of doses and in 1 child. Basophil activation did not differ before and after desensitization.

CONCLUSIONS. OIT induced desensitization with a clinically meaningful increase in peanut threshold.

REVIEWER COMMENTS. This large, well-designed clinical trial found comparable results to a double-blind, randomized, placebo-controlled study published in 2011. In the earlier study, 16 children in the treatment group (84%) completed 1 year of peanut OIT and tolerated a DBPCFC to 5000 mg of peanut protein, whereas the placebo group tolerated a median cumulative dose of 280 mg of peanut protein (Varshney P, Jones SM, Scurlock AM, et al. A randomized controlled study of peanut oral immunotherapy: clinical desensitization and modulation of the allergic response. J Allergy Clin Immunol. 2011;127[3]:654–660). The 2014 study used a lower cumulative DBPCFC dose (1400 mg) and did not mask group allocation to active treatment or placebo. Although this study did not exclude children with severe asthma or life-threatening reactions to peanut, the numbers of these high-risk children completing the study were not reported. Wheezing and laryngeal edema were not universally treated with intramuscular epinephrine. The 1 participant who used intramuscular epinephrine was withdrawn from the study.

Clinical Predictors for Favorable Outcomes in an Oral Immunotherapy Program for IgE-Mediated Cow’s Milk Allergy

PURPOSE OF THE STUDY. The goal of this study was to assess the safety and efficacy of milk oral immunotherapy (OIT) in milk-allergic children and adults, including high-risk patients.

STUDY POPULATION. The study included 280 Israeli patients, ages 4 to 27 years (median age: 7.5 years), with persistent cow’s milk allergy as defined by positive results on skin prick test and/or specific-serum IgE, positive oral food challenge, or history of clinical reaction with accidental exposure in the last 12 months. High-risk patients, including those with a history of anaphylaxis (as defined by involvement of at least 2 organ systems), were not excluded. In fact, 73% had a history of anaphylactic reaction. Patients with uncontrolled asthma were excluded.

METHODS. Using an open-label individualized treatment program, monthly rounds of OIT were administered by using fresh cow’s milk via a modified challenge-desensitization protocol. All patients were skin tested, with complete blood count and eosinophil counts obtained at the start of the program. The induction phase determined the maximal tolerated starting dose. This phase was performed in the hospital setting, with escalating doses of cow’s milk and observation for reactions with appropriate treatment. By the second day, 98% of patients had exhibited reactions. The third and fourth days were used to repeat the maximum tolerated starting dose and verify that it was safe. During the home dosing phase, the maximum tolerated starting dose was then given twice daily at home for 24 days.

RESULTS. Five patients failed milk OIT during induction, and 15 patients were still being studied. Sixty-two percent of the remaining patients (160 of 260) were able to freely consume milk (>7200 mg), and 25% were able to tolerate smaller amounts, with 85% consuming at least 180 mg of cow’s milk protein or the equivalent of 6 mL of milk. Clinically significant factors \( (P < .001) \) for achieving full tolerance to cow’s milk protein included a higher starting dose (odds ratio: 4.6 [for >30 mg]), not requiring epinephrine during induction (odds ratio: 5.2), and lack of anaphylactic reactions (odds ratio: 15.6).

CONCLUSIONS. This study presents clinical factors that may be helpful in predicting which patients undergoing milk OIT might be able to achieve full consumption of cow’s milk protein.

REVIEWER COMMENTS. Challenges exist to prescribing food OIT at this point due to several unresolved issues, and the approach is not currently approved. These challenges include optimal criteria for patient selection, timing and duration of treatment, and the optimal protocol to maximize safety and effectiveness. This study may help with patient selection and risk stratification. Even when subjects were unable to be successfully desensitized, they tolerated a “minimal protective dose.” This approach would offer some protection against accidental ingestions and would greatly increase the quality of life for a number of patients.
Assessing the Efficacy of Oral Immunotherapy for the Desensitisation of Peanut Allergy in Children (STOP II): A Phase 2 Randomised Controlled Trial

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