

Clinical Communications

Dosing, safety, and quality of life after peanut immunotherapy trials: A long-term follow-up study

Quindelyn Cook, MD^a, Luanna Yang, MD^a,
Ahmad Hamad, MD^a, Holly Barber, BSN^b,
Lauren Herlihy, CPNP^a, A. Wesley Burks, MD^a, and
Edwin H. Kim, MD^a

Clinical Implications

- Little is known about long-term effects of peanut immunotherapy. This study suggests that regular incorporation of dietary peanut following completion of immunotherapy can be beneficial, safe, and well tolerated based on parameters including accidental exposures, adverse reactions, and quality of life.

Oral immunotherapy (OIT) and sublingual immunotherapy (SLIT) have emerged as possible treatments for those affected by peanut allergy. Trials have demonstrated safety and efficacy,¹ but the ability to introduce peanut afterwards and its long-term effects have not been well described.^{2,3} At our center, upon completion of an immunotherapy protocol, all subjects demonstrating desensitization to greater than or equal to 300 mg of peanut were instructed to introduce dietary peanut and were invited to participate in this study. The Determining the Efficacy and Value of Immunotherapy on the Likelihood of Peanut Tolerance study (early peanut OIT trial) demonstrated that 300 mg of peanut protein provided comparable clinical outcomes to 3000 mg of protein with better tolerability.⁴ Based on these findings, 300 mg of daily peanut protein food was recommended following immunotherapy completion. Families that wished to push the dose higher could do so under close guidance.

One-hundred thirty past trial participants at the University of North Carolina were asked to complete a 21-point telephone survey that evaluated the following domains: peanut food characteristics, adverse reactions, accidental exposures, quality of life, and risk-taking behaviors. Fifty-five families out of 130 completed the survey. Median age at consent for the parent study was 3.5 years. There was a broad range of time from completion of the parent trial with a median of 2.9 years. Participants were mostly male (55%), white (94%), and previously enrolled in an OIT trial (73%) (Table I). Nonrespondents were of similar sex (males, 72%), but had a higher median age of 13.1 years at follow-up.

Forty-nine subjects (89%) continued peanut consumption at the time of survey. Most subjects consumed peanut daily (64%). The median quantity consumed was 600 mg. Past OIT participants consumed more peanut (mean dose, 955.6 mg; median, 600 mg) compared with SLIT participants (mean dose, 543.3 mg; median, 500 mg) (Figure 1, A). This was not statistically significant ($P = .13$). Older subjects consumed less peanut protein, but no significant correlation was noted between age and dose of peanut consumed ($r = -0.17$; $P = .27$). The preferred foods for peanut consumption were Reese's Pieces (30.5%), peanut M&M's (18.6%), peanuts (22%), peanut flour (6.8%),

peanut butter (11.9%), and miscellaneous candy bars/peanut cups (8.5%) (Figure 1, B).

Fourteen subjects (25%) reported at least 1 reaction within 2 hours of peanut ingestion. Cutaneous symptoms were most common (8 of 55); however, subjects also reported laryngeal/pulmonary (6 of 55), gastrointestinal (7 of 55), and oropharyngeal (5 of 55) symptoms (Figure 1, C). Antihistamines were most commonly used (11 of 55) compared with epinephrine (3 of 55), steroids (2 of 55), and albuterol (1 of 55). Three subjects (5%) had systemic reactions requiring epinephrine, of which 2 subjects subsequently stopped dietary peanut (Figure 1, D). But arguably, because 6 of 55 subjects did have pulmonary/laryngeal symptoms, epinephrine use was warranted. Our survey tool did not capture details regarding ancillary factors that may have affected reactions (ie, exercise). Ten of 14 subjects (71%) continued dietary peanut despite reactions. There was no difference in the amount of peanut ingested for subjects reporting reactions versus those without (mean 873 mg vs mean 885 mg, respectively). Six of 55 subjects (11%) stopped dietary peanut. Reasons for discontinuation included an eosinophilic esophagitis diagnosis (1 of 55), taste aversion (2 of 55), and allergic reactions (3 of 55). All the subjects who discontinued dietary peanut were in a parent OIT trial.

Parents of study subjects were asked to rate perceptions of safety. Ninety-eight percent of parents (54 of 55) "definitely" or "probably" felt that their child was safer following completion of immunotherapy. With regard to quality of life, 93% of parents (51 of 55) "definitely" or "probably" felt that their child's quality of life was improved following therapy. Similarly, 95% of parents (52 of 55) felt that their own personal quality of life was improved. Eighty-seven percent of subjects (48 of 55) were comfortable consuming products labeled "may contain peanut." In addition, 93% of subjects (51 of 55) felt more comfortable eating at restaurants and 87% of parents (48 of 55) were more comfortable with their children participating in unsupervised social settings. Interestingly, 50% of subjects (3 of 6) who discontinued home peanut dosing still reported a definite or probable improvement in all quality-of-life survey parameters. Meanwhile, 66% of subjects (36 of 55) reported allergies to at

TABLE I. Respondent characteristics

Characteristic	Value
Currently dosing peanut food, n of N (%)	49 of 55 (89)
Sex: male, n (%)	30 (55)
White, n (%)	52 (94)
Prior OIT trial participation, n (%)	40 (73)
Prior SLIT trial participation, n (%)	15 (27)
Median age at time of parent study consent (y)*	3.5 (1.5-13.9)
Median age at time of follow-up survey (y)*	10.8 (6.1-20.3)
Median time since study completion†	2.9 (1.2 mo-7.5 y)
Families who reported carrying emergency epinephrine "often," n (%)	47 (85)
Followed up with an allergist annually, n (%)	33 (60)

*Respondent ages are reported as medians with minimum and maximum ages at the time of parent study consent and time of contact for the follow-up survey.

†Median time (y) since parent study completion with range reported.

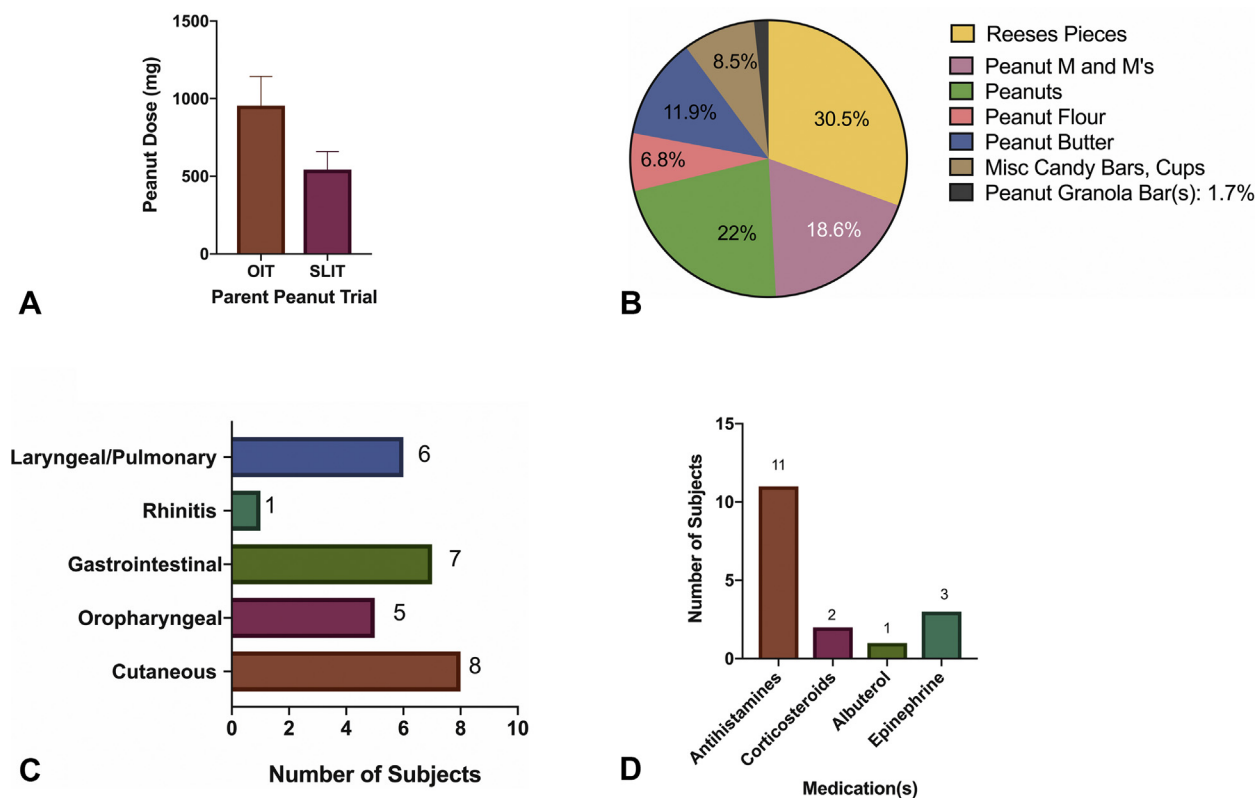


FIGURE 1. (A) Comparison of peanut food dose based on parent trial. This is a comparison of median peanut dose consumed based on parent trial. OIT subjects consumed more peanut (median, 600 mg; mean, 955 mg) in comparison to SLIT subjects (median, 500 mg; mean, 543 mg). (B) Types of peanut food vehicles. Most respondents consumed Reese's Pieces (30.5%), raw peanuts (22%), and peanut M & M's (18.6%). Less frequently used vehicles include peanut flour, peanut butter, miscellaneous candy bars/cups, and peanut-containing granola bars. (C) Symptoms of dose-related reactions. Fourteen subjects reported reactions within 2 hours of dosing home peanut. Cutaneous reactions were the most common (8 of 55 [14.5%]), followed by gastrointestinal symptoms (7 of 55 [12.7%]) and laryngeal/pulmonary (6 of 55 [10.9%]). (D) Treatment of reactions. Most reactions were treated with antihistamines (11 of 14 [78.6%]). Three of fifty-five subjects had reactions that required treatment with epinephrine. Two of those subjects stopped home dosing.

least 1 other food, but 100% of these individuals reported an improvement in safety and/or quality-of-life parameters. In looking at risk-taking behaviors, 85% of subjects (47 of 55) carried epinephrine autoinjectors "often" and 60% of subjects (33 of 55) saw an allergist annually (Table I). This is improved compared with rates seen among food-allergic individuals who have not undergone immunotherapy.⁵

There are limitations to this study including the presence of recall bias and lack of baseline quality-of-life data. A non-validated questionnaire administered via telephone survey was used, which did not allow for direct evaluation of peanut reactions or response. As mentioned previously, only 42% of families completed the survey, which introduces bias as well. We hypothesize that recent study completion and extremely motivated families were more willing to participate. Also, families who experienced an adverse reaction to home peanut might have been less willing to participate given their negative experience. As a result, we likely did not capture the full extent of reactions occurring with home peanut consumption. Other clinical data including peanut specific IgE, skin test results, or challenge data were not included in our analysis. Also, most participants received OIT, which could have artificially boosted

results because OIT has historically demonstrated more consistent efficacy compared with SLIT.^{1,6} This was reflected in our small pool of SLIT subjects being able to consume less peanut. The difference in response is likely because SLIT subjects are desensitized to a lower peanut dose compared with OIT due to the limitations imposed by using a liquid, sublingual vehicle. A strength to these data is that our center adds to the limited body of work surrounding life after immunotherapy trials.^{2,3}

In summary, completion of peanut immunotherapy trials was associated with improved perceptions of safety and life satisfaction in subjects and their parents. Benefit was seen even in individuals with other food allergies or who had discontinued home peanut ingestion possibly due to the experience gained from completion of a trial. Risk-taking behavior does not appear to be increased. Peanut consumption after immunotherapy is also well tolerated. With the recent Food and Drug Administration approval of Palforzia (AR101), an oral peanut immunotherapy product, this is particularly relevant to current clinical practice because self-administration of peanut at home may be a more realistic representation of how patients and families choose to maintain long-term desensitization. Proper counseling on the

importance of regular follow-up and the continued necessity of emergency medications is essential.

^aSchool of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC

^bSchool of Nursing, University of North Carolina, Chapel Hill, NC

No funding was received for this work.

Conflicts of interest: A. W. Burks owns stock in Allertein and Mastcell Pharmaceuticals; receives grant support to his institution from the National Institutes of Health and Food Allergy Research & Education; royalties from UpToDate; and consulting honorariums from Astella Pharma Global Development, DBV Technologies, kaléo, N-Fold, LLC, and UKKO, Inc, as well as Aimmune Therapeutics, Consortia TX, Inc, and Prota Therapeutics for his service on their respective scientific advisory boards. E. H. Kim reports consultancy with Aimmune Therapeutics, DBV Technologies, AllerGenis, Allakos, Ukko, and Vibrant America; and clinical medical advisory board membership with DBV technologies. Grant funding has been received by A. W. Burks from the National Institutes of Health, National Institute of Allergy and Infectious Diseases, NIH-National Center for Complementary and Integrative Health, Food Allergy Research & Education, and the Wallace Research Foundation. The rest of the authors report that they have no relevant conflicts of interest.

Received for publication November 18, 2019; revised April 6, 2020; accepted for publication April 6, 2020.

Available online ■ ■

Corresponding author: Edwin H. Kim, MD, 3004 Mary Ellen Jones Bldg, 116 Manning Dr, CB 8035, Chapel Hill, NC 27599. E-mail: edwinkim@email.unc.edu.

2213-2198

Published by Elsevier Inc. on behalf of the American Academy of Allergy, Asthma & Immunology

<https://doi.org/10.1016/j.jaip.2020.04.021>

REFERENCES

1. Gernez Y, Nowak-Wegrzyn A. Immunotherapy for food allergy: are we there yet? *J Allergy Clin Immunol Pract* 2017;5:250-72.
2. Nachshon L, Goldberg M, Katz Y, Levy M, Elizur A. Long-term outcome of peanut oral immunotherapy—real life experience. *Pediatr Allergy Immunol* 2018; 29:519-26.
3. Lewis MO, Brown-Whitehorn TF, Burke DD, Cianferoni A, Heiwall J, Reddy A, et al. Life after peanut immunotherapy. *J Allergy Clin Immunol* 2017;139:AB387.
4. Vickery BP, Berglund P, Burk CM, Fine JP, Kim EH, Kim JI, et al. Early oral immunotherapy in peanut-allergic preschool children is safe and highly effective. *J Allergy Clin Immunol* 2017;139:173-81.
5. Rudders SA, Banerji A, Vassallo MF, Clark S, Camargo CA. Trends in pediatric emergency department visits for food-induced anaphylaxis. *J Allergy Clin Immunol* 2010;126:385-8.
6. Cook QS, Kim EH. Update on peanut allergy: prevention and immunotherapy. *Allergy Asthma Proc* 2019;40:14-20.