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The Impact of Tree Nut Oral Food Challenges on Quality of Life and Acute Reactions in Nut Allergic Patients

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To the Editor,

Tree nut (TN) allergies are estimated to affect 0.1–4.3% of the population.¹ Current management of TN allergy is avoidance and emergency medications in the event of an accidental exposure. There is a high rate of cross-reactivity among the TNs and most individuals are allergic to more than one TN.² Furthermore, up to 50% of patients with peanut allergy are allergic to TNs.³ Standard skin or serologic testing does not always differentiate between cross-sensitization and clinical cross-reactivity.⁴ For these reasons, many providers recommend that peanut or TN allergic patients avoid all nuts, regardless of reaction history or test results. However, food restrictions and the fear of accidental food exposures may significantly impact quality of life (QOL).⁵

Another option for patients with suspected TN allergy is to undergo oral food challenges (OFC) to specific nuts, which can lead to a more targeted avoidance diet. We are not aware of evidence regarding the impact of TN OFCs and targeted avoidance with regard to QOL or risk of accidental exposures.

Therefore, we surveyed families to determine the impact of TN OFCs and selective nut avoidance on QOL and risk of reactions, comparing those who chose to undergo select TN OFCs compared to those who chose complete nut avoidance.

In our clinic, based on the combination of history, skin testing, and IgE results, TN OFCs are most often offered to patients estimated to have a high chance of a successful outcome.⁶ For this cross-sectional study, we contacted patients who had been offered a TN challenge if they: 1) underwent a TN OFC in the past 2 years, but are still avoiding at least one TN or peanut (group 1), or 2) declined a TN OFC and are avoiding all nuts (group 2). Participants

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Clinical Implications: Tree Nut oral food challenges and a targeted nut avoidance diet improve food allergy related quality of life in select groups.

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completed questionnaires on demographics, allergy history, food allergy related quality of life (FAQOL), and reasons for accepting or declining TN OFCs.

FaQOL was evaluated using validated questionnaires for parents (parent form: FaQOL-PF), children (child form: FAQOL-CF, 8–12 years), and/or teenagers (teenager form: FaQOL-TF, 13–17 years),^{7–9} which include specific domains for parents (emotional impact (EI), food anxiety (FA), social dietary limitations (SDL)), children (EI, allergen avoidance (AA), risk of accidental exposure (RAE), dietary restrictions (DR)) and teenagers (EI, AA, RAE). Each question was answered using a 7-point Likert scale (0–6). Lower scores indicate better FaQOL. We added a single yes/no question: “Overall, has your QOL improved since the TN OFC?”

Variables were compared by t test and Chi square for continuous and categorical variables, respectively. The clinical significance of FaQOL scores was assessed using a minimal clinically important difference (MCID), defined as the smallest difference that patients perceive as beneficial.¹⁰ For the 7-point Likert scale, prior studies have used an approximate mean difference (MD) of 0.5 for the MCID.¹⁰

Fifty-eight families completed questionnaires (group 1: 37, group 2: 21) (Table I). The mean age was 10 years. The sample was predominately male (59%), white/Caucasian (71%), with a high rate of co-morbid asthma (52%), allergic rhinitis (71%), eczema (83%), peanut allergy (84%), and other non-nut food allergies (59%). The mean age at TN allergy diagnosis was 17 months (range 3–84). Twenty-eight percent had a TN reaction history. The most common reason for TN testing was a reaction to a non-nut food.

We found no differences in demographics, co-morbid peanut or non-nut food allergy, other atopic disease, number of prior peanut or TN reactions, or proportion with a peanut or TN reaction history between groups 1 and 2 (Table I).

Thirty-seven children underwent a total of 122 TN OFCs (mean of 3.3 TNs/person, range 1–6). All challenges were performed at Johns Hopkins using a standard tree nut OFC protocol. Ninety-seven percent (36/37) of children passed to at least one TN, equating to a successful challenge to 114 of 122 TNs (93%). Eighty-nine percent (33/37) introduced at least one TN post-OFC, with 49% (18/37) introducing all challenged TNs. Reasons for not introducing TNs included difficulty finding non-cross-contaminated nuts, child dislike/preference, nut not regularly eaten in the home, family member with a nut allergy, and “easier to avoid.”

For group 1, the median duration of follow-up after the TN OFC was 11.8 months (range 1–30 months). During this period, there was one accidental TN reaction and no peanut reactions. Similarly, group 2 had no TN or peanut reactions in the 12 months prior to completing the survey. Of the 33 people in group 1 who introduced TNs after the OFC, five reported symptoms and then 4/5 returned to avoiding that TN (see Table EI in the Online Repository).

Fifty-eight parents, 18 children, and 10 teenagers completed FaQOL questionnaires. Twenty-one children were <8 years and did not complete the FaQOL (Table II). Parent data showed no clinically meaningful difference between groups 1 and 2. Children reported

higher FAQOL scores in group 1 versus group 2, indicating a potentially negative impact of food allergy in those who underwent a TN OFC. However, teenagers reported opposite results with lower overall, EI, and RAE FAQOL scores in group 1 versus group 2. All respondents answered yes to the question, “Overall, has your QOL improved since the TN OFC?”

Given that other non-TN food allergies might also affect FaQOL scores, we re-assessed parent results by the number of non-TN food allergies (<3 or ≥3 foods). In group 1, those with <3 other food allergies had a significantly lower FaQOL score than those with ≥3 (1.9 vs 2.9, MD: −1). This same difference was not seen in group 2 (2.76 vs 2.48, MD: 0.28). Similarly, when comparing those with <3 other food allergies, group 1 had a lower FaQOL score than group 2 (1.9 vs 2.76, MD: −0.86).

Families had a variety of reasons for wanting or declining a TN OFC. Reasons for wanting an OFC included expanding the diet, clarifying the diagnosis, and decreasing worry. Top reasons for declining OFCs were fear/worry, lack of importance, and low likelihood of home nut introduction given other food allergies in the child or family members.

In summary, although patterns of FaQOL were inconsistent between groups, there may be an improved FaQOL in those undergoing TN OFCs, especially in teenagers and those with fewer other food allergies. For many families, TN OFCs may be beneficial in clarifying a diagnosis, decreasing uncertainty, and expanding the diet. If the specific TNs to be challenged are chosen carefully, the procedure is extremely safe as evidenced by our 93% success rate. In addition, although post-challenge data are limited by our relatively short follow-up time and small sample size, especially teenagers, introduction of TNs did not appear to increase the rate of accidental peanut or TN reactions. However, we also identified 5 patients with possible reactions post-OFC to a “safe” TN, which may be due to pollen-food allergy syndrome or an evolving allergy. In the overall analysis, while we never object if a family prefers to follow a “No Nut” diet, in most instances the benefits of selected TN challenges, especially with regard to FAQOL, appear to outweigh the risks.

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References:

1. Weinberger T, Sicherer S. Current perspectives on tree nut allergy: a review. *J Asthma Allergy*. 2018 3 26;11:41–51. [PubMed: 29618933]
2. Kazatsky AM, Wood RA. Classification of Food Allergens and Cross-Reactivity. *Curr Allergy Asthma Rep*. 2016 3;16(3):22. [PubMed: 26874850]
3. Sampson HA, Aceves S, Bock SA, James J, Jones S, Lang D, et al. Food allergy: a practice parameter update-2014. *J Allergy Clin Immunol*. 2014 11;134(5):1016–25.e43. [PubMed: 25174862]
4. Eigenmann PA, Lack G, Mazon A, Nieto A, Haddad D, Brough HA, et al. Managing Nut Allergy: A Remaining Clinical Challenge. *J Allergy Clin Immunol Pract*. 2017 3;5(2):296–300. [PubMed: 27793601]

5. Cummings AJ, Knibb RC, King RM, Lucas JS. The psychosocial impact of food allergy and food hypersensitivity in children, adolescents and their families: a review. *Allergy*. 2010 8;65(8):933–945. [PubMed: 20180792]
6. Fleischer DM, Conover-Walker MK, Matsui EC, Wood RA. The natural history of tree nut allergy. *J Allergy Clin Immunol*. 2005 11;116(5):1087–1093. [PubMed: 16275381]
7. DunnGalvin A, Cullinane C, Daly DA, Flokstra-de Blok BM, Dubois AE, Hourihane JO. Longitudinal validity and responsiveness of the Food Allergy Quality of Life Questionnaire-Parent Form in children 0–12 years following positive and negative food challenges. *Clin Exp Allergy*. 2010 3;40(3):476–485. [PubMed: 20210816]
8. Flokstra-de Blok BM, DunnGalvin A, Vlieg-Boerstra BJ, Oude Elberink JN, Duiverman EJ, Hourihane JO, et al. Development and validation of a self-administered Food Allergy Quality of Life Questionnaire for children. *Clin Exp Allergy*. 2009 1;39(1):127–137. [PubMed: 19016799]
9. Flokstra-de Blok BM, DunnGalvin A, Vlieg-Boerstra BJ, Oude Elberink JN, Duiverman EJ, Hourihane JO, et al. Development and validation of the self-administered Food Allergy Quality of Life Questionnaire for adolescents. *J Allergy Clin Immunol*. 2008 7;122(1):139–44, 144.e1–2. [PubMed: 18602570]
10. Jaeschke R, Singer J, Guyatt GH. Measurement of health status. Ascertaining the minimal clinically important difference. *Control Clin Trials*. 1989 12;10(4):407–415. [PubMed: 2691207]

Table I:**Patient Characteristics**

	All	Group 1	Group 2
N	58	37	21
Age (years)	9.7	9.5	10.1
Male: n (%)	34 (59%)	23 (62%)	11 (52%)
Race: n (%)			
- White/Caucasian	41 (71%)	25 (68%)	16 (76%)
- Black/African American	5 (9%)	4 (11%)	1 (5%)
- Asian	1 (2%)	1 (3%)	0
- Other	11 (19%)	7 (19%)	4 (19%)
Other Atopic Disease: n (%)			
- Asthma	30 (52%)	17 (46%)	13 (62%)
- Allergic rhinitis	41 (71%)	23 (62%)	18 (86%)
- Eczema	48 (83%)	32 (86%)	16 (76%)
Household member with nut allergy: n (%)	14 (24%)	9 (24%)	5 (24%)
Age at TN allergy diagnosis (months): mean (range)	17 (3–84)	16 (3–60)	20 (6–84)
Reason(s) tested for a TN allergy: n (%)			
- Reaction to tree nut	11 (19%)	5 (14%)	6 (29%)
- Reaction to peanut	16 (28%)	10 (27%)	6 (29%)
- Reaction to non-nut food	20 (34%)	15 (41%)	5 (24%)
- Eczema	8 (14%)	5 (14%)	3 (14%)
- Family history of nut allergy	2 (3%)	2 (5%)	0%
- Other reason	12 (21%)	6 (16%)	6 (29%)
Tree Nut Reaction History			
- TN reaction history (yes/no): n (%)	16 (28%)	10 (27%) pre-TN OFC	6 (29%)
- Number lifetime TN reactions: mean (range)	0.60 (0–4)	0.62 (0–4)	0.57 (0–4)
Peanut Reaction History			
- PN reaction (yes/no): n (%)	29 (50%)	20 (54%)	9 (43%)
- Number of lifetime PN reactions: mean (range)	0.76 (0–7)	0.86 (0–7)	0.57 (0–3)
Other Food Allergies			
- Peanut allergy: n (%)	49 (84%)	32 (86%)	17 (81%)
- Non-Nut food allergies (yes/no): n (%)	34 (59%)	21 (57%)	13 (62%)
- Number of non-nut food allergies (mean, range)	1.8 (0–9)	1.9 (0–9)	1.6 (0–4)
- <3 Non-Nut food allergies: n (%)	27 (47%)	17 (46%)	10 (48%)
Parent Education (n, %)			
- Less than high school	1 (2%)	0	1 (5%)
- high school	2 (3%)	2 (5%)	0
- college	15 (26%)	8 (22%)	7 (33%)
- post-college	40 (69%)	27 (73%)	13 (62%)

- $P > 0.05$ for all variables

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Table II.

Food Allergy Quality of Life Mean Scores in Group 1 and Group 2

	Group 1	Group 2	Mean Difference (95% CI)
Parent Form			
n	37	21	
Total Score	2.45	2.61	-0.16 (-0.82-0.49)
Emotional Impact	2.25	2.38	-0.13 (-0.73-0.47)
Food Anxiety	2.71	2.81	-0.1 (-0.89-0.67)
Social Dietary Limitation	2.50	2.72	-0.22 (-1.04-0.6)
Child Form			
n	12	6	
Total Score	3.83	3.30	+0.53 (-0.90-1.96)
Emotional Impact	4.04	3.25	+0.79 (-0.93-2.51)
Allergen avoidance	3.88	3.21	+0.67 (-0.80-2.14)
Risk of accidental exposure	3.67	3.33	+0.34 (-1.03-1.69)
Dietary restriction	3.75	3.41	+0.33 (-1.30-1.96)
Teenager Form			
n	7	3	
Total Score	2.74	3.44	-0.7 (-2.30-0.91)
Emotional Impact	2.48	4.04	-1.55 (-3.37-0.27)
Allergen avoidance	2.86	2.97	-0.11 (-2.19-1.97)
Risk of accidental exposure	2.86	3.5	-0.64 (-2.31-1.02)

* A lower score indicates better food allergy-related QOL. We calculated the difference between group 1 and group 2. Hence, a negative mean difference indicates better food allergy-related QOL in group 1.

Online Repository Table E1.

Patients with a Tree Nut reaction after Negative Tree Nut OFC

Pt	age at OFC sex	Nuts	Time of reaction from OFC	Symptoms
1	10 male	walnut, hazelnut, pecan	<1 month	For about 1 month post-OFC, <u>oral pruritus</u> with eating walnut, pecan, and hazelnut. Now eats with no symptoms.
2 *	9 female	almond	8 months	Ate almonds daily for 8 months. <u>Oral pruritus, chest tightness, difficulty breathing</u> after eating handful of almonds. Received epinephrine, antihistamine, and steroids. Now avoiding all tree nuts.
3	8 male	almond	1–2 months	<u>Oral pruritus and abdominal pain</u> after eating almond approx. 3 times. No medications given. Now avoiding almond (eating pine nut, brazil nut, hazelnut, pecan)
4	16 female	pistachio	8 months	<u>Oral pruritus, abdominal pain</u> after eating a tiny piece of pistachio. Received antihistamine. Avoiding pistachio, but eats cashew and almond.
5	9 male	hazelnut	2 months	<u>Oral pruritus</u> after eating hazelnut spread. No medications given. Now avoids hazelnut. Eats almond.

Patients 1–5 had symptoms to a TN introduced at home after a successful in office challenge.

* Patient 2- After a follow-up evaluation, it was felt that she likely had an oral allergy type reaction, which then triggered anxiety. A repeat OFC has been offered.