Clinical experience with sesame oral immunotherapy and a quality-of-life assessment

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ABSTRACT

Background: *Allergic reactions to sesame have increased in prevalence in the United States. Sesame oral immunotherapy (OIT) is an emerging management strategy. Few reports assessed the benefits and risks of sesame OIT in children with sesame allergy.*

Objective: *To study the adverse events and quality of life (QoL) on sesame OIT in a U.S. population.*

Methods: *Twenty-three patient charts were retrospectively reviewed from 2017 to 2020. The patients received a validated Food Allergy Quality of Life Questionnaire and a survey on adverse reactions during maintenance therapy. Patients who were 8.5 ± 4.7 years of age (30% girls and 70% boys) with a documented history of sesame allergy and who had undergone sesame OIT were reviewed.*

Results: *The buildup phase was 293.7 ± 87.1 days. Twenty-one of the 23 patients (91.3%) reached maintenance therapy. Twenty-one patients (91.3%) had at least one gastrointestinal reaction; 18 (78.3%) had at least one cutaneous reaction; 6 (26%) had at least one respiratory reaction. Age raised the odds of gastrointestinal reactions more than fivefold (odds ratio [OR] 5.653 (95% confidence interval [CI], 2.409 – 13.269); p = 0.0009). Asthma boosted the odds of respiratory reactions of more than ninefold (OR 9.206 [95% CI, 1.535 – 55.211]; p = 0.0187). Female gender increased the odds of having a respiratory reaction by more than sevenfold (OR 7.545 [95% CI, 1.207 – 47.153]; p = 0.0330). Asthma amplified the odds of cutaneous reactions (OR 11.725 [95% CI, 2.390 – 57.517]; p = 0.0053). Three patients ultimately discontinued therapy. Food-related anxiety (–0.773) and social/dietary limitation (–0.687) improved significantly in QoL.*

Conclusion: *Sesame OIT may be safe and easily adaptable to private practice and significantly improves QoL. Further prospective studies would be helpful to fully assess these relationships.*

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Sesame is the oldest oilseed crop known to humanity.[1] Its allergy prevalence rates are now similar to other common allergens, *e.g.*, soy and pistachio.[2] However, sesame lacks the same institutional safety mechanisms. Although sesame is an allergen for 0.2%-0.8% of the U.S. population, it remains an optional label until the implementation of the FASTER Act in 2023, which will require manufacturers to label sesame exposure.[3–6] Managing sesame allergy can result in a significant emotional and physical burden on patients and their families given its incorporation in many foods.[5,7] Oral immunotherapy (OIT) may mitigate that burden, which decreases the risk of severe allergic reactions and increases quality of life (QoL).[4,8–11]

However, OIT is not without a risk of adverse reactions (AR), which can range from mild gastrointestinal symptoms to severe anaphylaxis. In addition, eosinophilic gastrointestinal disease is an uncommon, potential complication of therapy.[12,13] Logistically, OIT requires infrastructure, specially trained staff, and oversight of an allergist as well as long-term, intensive time and financial commitment by patients and their families.[13] This retrospective review examined patients who received OIT at a community-based food allergy treatment center. To our knowledge, it is the first U.S. report of patients treated with sesame OIT. This analysis examined the risk factors for ARs, the percentage of patients who reached maintenance therapy, and any associated ARs as well as the impact of sesame OIT on QoL.

METHODS

This retrospective study was conducted at the New England Food Allergy Treatment Center, West Hartford, Connecticut. Twenty-eight patients with sesame allergy,

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who were treated with OIT between 2017 and 2020, were identified, and informed consent was obtained. Patients were diagnosed with sesame allergy if they had either a convincing history of an allergic reaction plus a positive skin-prick test result to sesame or positive oral food challenge (OFC) result to sesame. Patients were tested for serum specific sesame immunoglobulin E (IgE) before starting OIT. During treatment, ARs were defined as cutaneous, gastrointestinal, respiratory, and systemic symptoms that departed from baseline after ingestion of sesame at any dose.[14] Families recorded their child's ARs by using a daily diary, which the staff reviewed at every induction visit. Induction was defined as the subsequent step-up sesame protein doses in the clinical regimen that required medical observation for patient safety.

The patients received daily doses of sesame flour, obtained from Dipasa USA, Inc, Brownsville, Texas, USA and then transitioned at 500 mg to tahini or Joyva Marble Halvah, produced by Joyva Corporation, Brooklyn, New York, USA (Fig. 1). Sesame flour was increased every 2 weeks as tolerated during the buildup until a maintenance dose was reached. Every clinic visit included a screening for eosinophilic esophagitis (EoE). In the absence of a consensus on optimal dosing for sesame OIT, there was a variance in the maintenance dose based on clinical experience and that of other researchers. Over the time period encompassed in the review, the maintenance dose was lowered from 1000 mg to 400–600 mg based on new literature and clinical experience.[15] If more than three consecutive doses were missed, then the patients were instructed to call the center for instructions. Most frequently, based on medical expertise for patient safety, the prescribed dose was halved for the remainder of the week and then the patient was told to restart the prescribed dose for the preset allotted time; this resulted in a prolonged buildup phase for some patients. In response to ARs, the patients were told to remain on the current dose rather than updose. The patients were advised to avoid physical exertion for 2 hours after dosing and to hold a dose in an event of a febrile illness or poorly controlled asthma. In addition, it was recommended that the patients consume their dose with a carbohydrate meal. Follow-up OFCs were not routinely performed to assess the level of desensitization based on parent choice and the goal of the study.

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NEFATC SESAME PROTOCOL

Visit	Dose Sesame Protein (mg)		
Day 1 - Dose 1	0.1 mg		
Day 1 - Dose 2	0.2 mg		
Day 1 - Dose 3	0.4 mg		
Day 1 - Dose 4	0.8 mg		
Day 1 - Dose 5	1.5 mg		
Day 1 - Dose 6	3 mg		
V2	3 mg		
V3	4.5 mg		
V4	6 mg		
V5	9 mg		
V6	12 mg		
V7	18 mg		
V8	25 mg		
V9	35 mg		
V10	50 mg		
V11	75 mg		
V 12	100 mg		
V13	125 mg		
V14	165 mg		
V15	225mg		
V16	300 mg		
V17	400 mg **(Last dose of flour)**		
V18	Tahini **(target 500 mg protein)**	Joyva Marble Halvah **(500 mg protein)**	Joyva Marble Halvah Bar **(500mg protein)**
V19	Tahini **(target 600 mg protein)**	Joyva Marble Halvah **(600 mg protein)**	Joyva Marble Halvah **(600mg protein)**

Figure 1. *Sesame oral immunotherapy protocol. Dosing at subsequent visits was subject to change, depending on patient reactions to previous dosing: either the dose remained the same or was reduced to a previous dose of this protocol.*

Data Collection

Yale Institutional Review Board approved this retrospective review (2000028463). Data were collected on patients' demographics (history of nonsesame allergies, atopic disease, age, gender, age of sesame allergy diagnosis), history of sesame allergy, confirmatory sesame allergy testing, the presence of other atopic and allergic conditions, sesame OIT initiation date, maintenance date, discontinuation date, and reasons for dup and maintenance phases, any ARs, any new gastrointestinal medications, and new diagnoses of EoE were included. Epinephrine use and the need for a physician, urgent care, or emergency department visit for systemic reactions were recorded. If present, any patient-reported triggers for systemic reactions were recorded. Patients were excluded if they were still undergoing or had incomplete data for the buildup phase and if undergoing multiple OITs.

QoL data were collected *via* Yale Qualtrics, a secure survey platform powered by Qualtrics XM, Seattle, WA and Provo, UT, USA. The Food Allergy Quality of Life Questionnaires (FAQLQ) used were well-established surveys for patients with food allergy and their families.[16–22] FAQLQ was given by New England Food Allergy Treatment Center (NETAFC) before the patient's first OIT. As part of this study, the participants were given the FAQLQ after sesame OIT. We only used questions with individual responses that we could correlate before and after the buildup phase OIT; the responses were based on a Likert scale, and the difference was obtained by subtracting the responses. A positive difference indicated worsening perception and a negative difference indicated improving perception. Each difference was compared with the minimally clinically important difference (MID), a ± 0.5 unit change on the 7-point Likert scale.[23] The FAQLQ-parent consisted of 30 questions split into four domains: emotional impact, food-related anxiety, social/

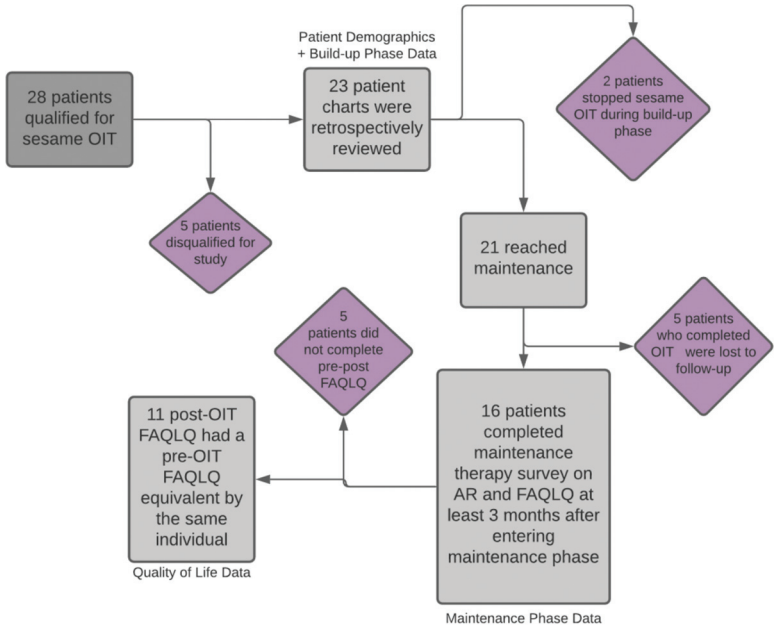

Figure 2. *Consort patient flow diagram and study plot schema. Five patients were disqualified. Two patients chose to discontinue sesame OIT because OIT was too time intensive or affected the patient's sleep and emotional state. The 3-month waiting period was a predetermined cutoff for administering the maintenance survey and FAQLQ based on the 6-month follow-up for patients who reached maintenance therapy. OIT = Oral immunotherapy; FAQLQ = Food Allergy Quality of Life Questionnaire.*

dietary limitation, and food safety. The domains were considered statistically significant if the mean of the differences in responses was greater than the MID. The survey was split into sections by applying to specific age groups.

Statistical Analysis

Clinical histories were summarized by using mean ± standard deviation (SD), frequencies, and proportions. Unadjusted associations among ARs and patient demographics and sesame IgE levels were examined by using multivariable logistic regression. In both phases, the primary outcomes of interest were the percentage of patients who experienced ARs; the odds ratios (OR) between total ARs, systemic reactions, and IgE values; ORs of single-system based ARs and IgE value, age, gender, eczema, asthma, or duration of sesame OIT; and usage of epinephrine and/or antihistamine and/or the emergency department during sesame OIT. Secondary outcomes were reasons for discontinuation and QoL.

Continuous variables were tested for linearity *via* visualization of basic plot diagrams and were discarded from the model if not linear. Categorical variables were always retained in the model. Potential multicollinearity was checked by examining bivariable associations among predictors by using either the χ^2 test, one-tailed or two-tailed *t*-test. Variables were retained at α of 0.05. Results were summarized by using ORs and 95% confidence intervals (CI). Analysis was done by using RStudio, Boston, MA, PBC version 1.3.1093. For QoL analysis, Microsoft Excel, Microsoft Corportion, Redmond, WA, was used to analyze means ± SDs, and ± standard errors. All graphs and figures were made *via* Microsoft Office or Lucidchart, Lucid Software Inc., South Jordan, UT.

RESULTS

As shown in Fig. 2, five patients were excluded: two patients had incomplete data and three patients were still undergoing the buildup phase. Thus, 23 charts were retrospectively reviewed. In total, 21 patients were in the maintenance phase during the time of our study; 91.3% of the eligible patients (21/23) reached maintenance therapy and 13% (3/23) withdrew within 1 year of the buildup and within 9 months of the maintenance phases.

Patient Characteristics

As shown in Table 1, at initiation, the mean ± SD age was 8.5 ± 4.7 years and all the patients were ages < 18 years. Thirty percent of the patients were girls. The mean ± SD age of sesame allergy onset was 4.0 ± 4.2 years. Seventy-eight percent of the patients reported a previous clinical reaction to sesame, which required epinephrine, antihistamines, or other medical treatment, or a visit to a medical professional. Ninety-six percent of the patients had concurrent food allergies: 69.57% had peanut allergies (16/23), 69.57% had allergies to tree nuts (16/23), and 47.83% had allergies to other foods (*e.g.*, seafood, eggs, chickpeas) (11/23). Twenty-two percent of the patients had environmental allergies (5/23), and 26% had drug allergies (6/23). Forty-four percent had asthma (10/23), and 70% had atopic dermatitis (16/23), whereas 35% had both (8/23). The mean ± SD size of the pre-OIT skin-prick test result was 15.7 ± 7.3 mm for the wheal (range, 5–35 mm) and 29.1 ± 7.7 mm

Table 1 **Patient clinical characteristics (*N* = 23)**

Characteristic	Value
Age, mean ± SD (min-max), y (mode)	8.53 ± 4.69, (1.19 - 18.51), 5 yrs
Girls/boys, %	30.43/69.57
Characteristics of sesame allergy before OIT initiation	
Patient's age at sesame allergy onset (*n* = 21), y	
Mean ± SD (min-max), y (mode)	3.99 ± 4.22 (0.8 - 12), 0.9 yrs
Mode	0.9
Median	2
Patients with previous clinical allergic reaction to sesame, % (*n*)	78.26 (18)
Patients who required epinephrine for a previous sesame reaction, % (*n*)	34.78 (8)
Patients who required an ED visit for a previous sesame reaction, % (*n*)	Unknown
Associated atopic conditions	
Patients with other food allergies, % (*n*)	95.65 (22)
Peanuts	69.57 (16)
Other nuts (*e.g.*, tree nuts, walnuts, cashews)	69.57 (16)
Other food allergies (*e.g.*, seafood, eggs, chick peas)	47.83 (11)
Patients with allergic rhinitis, % (*n*)	21.74 (5)
Patients with asthma, % (*n*)	43.48 (10)
Patients with atopic dermatitis, % (*n*)	69.57 (16)
Pre-OIT testing	
SPT wheal, range (flare, range) (*n* = 20), mean ± SD, mm	15.7 ± 7.3, 5–35 (29.1 ± 7.7, 16–45)
Sesame specific IgE value (range) (*n* = 22), mean ± SD, kU/L	18.63 ± 25.37 (0.71 to 100)
Sesame oral food challenge: taken; failed (*n* = 22), *n* (%)	10 (45.5); 10 (45.5)

SD = Standard deviation; OIT = oral immunotherapy; ED = emergency department; SPT = skin-prick test; IgE = immunoglobulin E.

for the flare (range, 16–45 mm). The mean ± SD value for the pre-OIT serum sesame IgE value was 18.6 ± 25.4 kU/L (range, 0.71–100 kU/L). OFC was administered to 45.5% of the patients with positive result (10/22); 54.5% of the patients did not receive OFC (12/22).

ARs during OIT

The mean ± SD duration of the buildup phase was 293.74 ± 87.12 days. During this phase, 21 patients (91.3%) had gastrointestinal symptoms, 18 (78.3%) had cutaneous symptoms, and 6 (26%) had respiratory reactions. Systemic reactions were 0.513% of all ARs and occurred in one patient (4.3%). A total of 39 ARs occurred with 567 clinic doses (6.88%), and 156 ARs occurred with 6305 home doses (2.47%). No emergency department visits, urgent care visits, hospitalizations, or fatalities occurred. One systemic reaction, of 195 ARs, was treated with a single dose of epinephrine. Other characteristics of ARs during the buildup are presented in Table 2: 66% of the ARs were gastrointestinal, 23.59% were cutaneous, and 8.71% were respiratory.

As shown in Table 3, increasing sesame IgE levels raised the odds of having one systemic reaction (OR 1.009 [95% CI, 1.004–1.014]; $p = 0.0008$). Increasing age amplified the odds of gastrointestinal reactions more than fivefold (OR 5.653 [95% CI, 2.409–13.269]; $p = 0.0009$), when controlling for IgE, gender, asthma, atopic dermatitis, and duration of therapy. Female gender augmented the odds of having a respiratory reaction by more than sevenfold (OR 7.545 [95% CI, 1.207– 47.153]; $p = 0.0330$). Asthma boosted the odds of respiratory reactions more than ninefold (OR 9.206 [95% CI, 1.535–55.211]; $p = 0.0187$), when controlling for gender and atopic dermatitis. Asthma increased the odds of cutaneous reactions 11-fold (OR 11.725 [95% CI, 2.390–57.517]; $p = 0.0053$).

The patients who reached maintenance took this dose indefinitely. Sixteen patients were available for follow-up; all the patients were at least 3 months into their maintenance phase (Fig. 2). The maintenance doses were the following: three patients were on 1000 mg; five patients were on 600 mg; six patients were on 500 mg; one patient was on 400 mg; and one patient was on 500 mg before withdrawing from her multi-OIT treatments. The final doses were determined by allergists and medical staff with input from the patient and family on health goals. Two systemic reactions (12.5%) were reported during maintenance. One patient reported using epinephrine and visited the emergency department. The other patient used epinephrine, followed up with a medical visit, and

Table 2 **Characteristics of single-system ARs during buildup phases (*N* = 23)**

Characteristic	Patients with at Least One Episode, *n* (%)	No. Episodes Reported per Patient
Gastrointestinal symptoms	21 (91.3)	129/195 total ARs (66.15%)
Abdominal pain	8 (35)	9.1 ± 11.2*
Oral itch	6 (26)	10.2 ± 11.9*
Vomiting	4 (17)	3.0 ± 2.2*
Nausea	1 (4)	6.0
Diarrhea	2 (9)	1.5 ± 0.7*
Difficulty swallowing	1 (4)	2.0
Other#	1 (4)	1.0
Cutaneous symptoms	18 (78)	46 of 195 (23.59)
Hives	12 (52)	3.1 ± 2.5*
Angioedema	1 (4)	1.0
Atopic dermatitis	2 (9)	6.0 ± 4.2*
Skin itching	1 (4)	1.0
Itchy eyes	1 (4)	1.0
Other#	1 (4)	1.0
Respiratory symptoms	6 (26)	17 of 195 (8.71)
Chest tightness	1 (4)	2.0
Wheezing	2 (9)	4.5 ± 4.95*
Coughing	2 (9)	2.5 ± 2.2*
Other#	1 (4)	1.0

AR = Adverse reaction; SD = standard deviation.
Percentages were rounded to the nearest whole number.
**Mean ± SD.*
#Uncategorized symptoms.

then discontinued OIT. No patients in our study were diagnosed with EoE. Characteristics of ARs and other calculated results are detailed in Tables 4 and 5, respectively. For every month increase in duration of maintenance, there were increased odds of gastrointestinal reactions (OR 2.036 [95% CI, 1.040 – 3.989]; $p = 0.04$).

QoL Assessments

In this study, 11 parents had completed FAQLQs surveys, comparative results of which are shown in Fig. 3 We received a 70% response rate (16/23). Of these, two domains were statistically significant: food-related anxiety (–0.773) and social/dietary limitation (–0.687). Within the former, questions that improved were children's "[concern] by poor labeling on food products" (Q29: –1.40) followed by children feeling "concerned that [parents are] worried that they will have a reaction to food" (Q5: –0.818). In the same domain, six other questions showed a greater than MID 0.5-unit improvement. Within 'social and dietary limitations,' the questions that improved were whether children were 'upset that family social outings (eating out, celebrations, *etc.*) have been limited by food allergy" (Q19: –1.444), followed by whether children felt limited by "restaurants we can safely go to as a family" (Q12: –1.364). Seven questions showed a greater than MID 0.5-unit improvement. In terms of restricted foods, families avoided fewer foods with the mode, moving from ≥10 foods to 3–6 foods that required avoidance. "Emotional impact" and "food safety" did not significantly change.

DISCUSSION

The increased prevalence of sesame allergy highlights an unmet need. OIT has been shown as an effective management strategy for patients with peanut and other food allergies.[10,13,24] To date, there is only one published report in the literature of sesame OIT.[4] To our knowledge, our analysis was the first U.S. review of ARs and QoL of patients treated with OIT conducted in a clinical practice setting. NEFATC's success in reaching the maintenance dose of sesame OIT, 90.9%, was comparable with previously reported studies.[4,10] ARs, particularly gastrointestinal symptoms, occurred at a higher rate than other reports[4]; however, there were fewer severe ARs, as evidenced by the reduced frequency of the requirements for epinephrine

Table 3 **Multivariable regressions for ARs in the buildup phase (N = 23)**

Parameter	n (%)*	Multivariable OR (95% CI)	p
Total AR			
IgE	22 (95)	0.983 (0.831 – 1.163)	0.8341
IgE#	18 (78)	1.542 (0.618 – 3.844)	0.3300
Systemic AR			
IgE	22 (95)	1.009 (1.004 – 1.014)	0.0008§
Gastrointestinal AR#			
IgE	18 (78)	1.277 (0.630 – 2.587)	0.4626
Age	18 (78)	5.653 (2.409 – 13.269)	0.0009§
Female	18 (78)	0.006 (0.000006 – 5.560)	0.1271
Asthma	18 (78)	0.091 (0.00012 – 68.299)	0.4425
Atopic dermatitis	18 (78)	111.658 (0.096 – 129885.80)	0.1695
Duration	18 (78)	3.927 (0.696 – 22.163)	0.1098
Respiratory AR# ¶			
Female	18 (78)	7.545 (1.207 – 47.153)	0.0330‖
Asthma	18 (78)	9.206 (1.535 – 55.211)	0.0187‖
Atopic dermatitis	18 (78)	0.803 (0.134 – 4.813)	0.7962
Cutaneous AR# **			
Female	18 (78)	1.993 (0.388 – 10.224)	0.3790
Asthma	18 (78)	11.725 (2.390 – 57.517)	0.0053##
Atopic dermatitis	18 (78)	0.638 (0.126 – 3.219)	0.5587
Duration	18 (78)	0.971 (0.675 – 1.396)	0.8621

AR = Adverse reaction; OR = odds ratio; CI = confidence interval; IgE = immunoglobulin E.
**Percentages were rounded to the nearest whole number.*
#Four patients with sesame IgE outliers were removed when evaluating ORs for total ARs and single-system ARs.
§High significance.
¶IgE, age, and duration were not linear.
‖Significance.
***IgE and age were not linear.*
##High significance.

Table 4 **Characteristics of adverse reactions during the maintenance phase (n = 16)**

Characteristic	Patients with at Least One Episode, n (%)	No. Episodes Reported per Patient, mean minimum − mean maximum
Systemic reactions	2 (12.5)	1 (no range)
Gastrointestinal reactions	4 (25)	
Abdominal pain	3 (17.6)	4–6
Diarrhea	1 (5.88)	1–3
Cutaneous reactions	6 (37.5)	
Hives	4 (23.5)	2.5–4.5
Atopic dermatitis	2 (11.6)	≥10 (no range)
Respiratory reactions	1 (6.25)	
Wheezing	1 (5.88)	7–9
Other: no adverse reactions	7 (41.2)	

use; our reliance on parental reports of ARs may explain the discrepancy.

Notably during the buildup, our AR occurrence percentage of induction doses, 6.88% (39/567), and home doses, 2.47% (156/6305), was comparable with the 4.7% (127/2720) and 2% (253/13170) in the Israeli study.[4] Six of the 23 patients experienced at least one AR during the first induction day of OIT in

Table 5 **Multivariable regressions of ARs during the maintenance phase (n = 16)**

Parameter	Multivariable OR (95% CI)	p
Total AR		
IgE	0.969 (0.893 – 1.052)	0.4276
Systemic AR		
IgE	Plot was not linear.	
Gastrointestinal AR#		
Female	6.054 (0.358 – 102.413)	0.1887
Asthma	0.227 (0.013 – 4.003)	0.2798
Atopic dermatitis	2.271 (0.139 – 37.103)	0.5314
Duration	2.036 (1.040 – 3.989)	0.0400*
Respiratory AR¶		
Female	1.396 (0.569 – 3.421)	0.4340
Asthma	1.429 (0.572 – 3.57)	0.4120
Atopic dermatitis	1.363 (0.577 – 3.220)	0.4480
Cutaneous AR¶		
Female	0.574 (0.062 – 5.303)	0.5962
Asthma	8.939 (0.921 – 86.781)	0.0576
Atopic dermatitis	2.011 (0.238 – 16.963)	0.4892

AR = Adverse reaction; OR = odds ratio; CI = confidence interval; IgE = immunoglobulin E.
#IgE and age were not linear.
**Significant p-value.*
¶IgE, age, and duration were not linear.

comparison with 58 of 60 patients in the aforementioned analysis. One patient (4.34%) was administered epinephrine for 1 of 195 ARs (0.5%) in comparison with 15 patients (25%) for 20 of 380 home and induction ARs (5.26%) in a previous study.[4] Not surprisingly, given atopy progression, a significant positive relationship existed between asthma and frequency of cutaneous reactions. Asthma, age, IgE level, and gender were the strongest factors that increased the risk for an AR.

Analysis of the QoL data was revealing. Patients with multiple allergies (95.6%) may show less improvement in QoL because these patients are coping with other food allergies in comparison with their single allergy counterparts.[25] In fact, a single-food allergy and worse baseline QoL predicted greater improvement in QoL after OIT when analyzing a group of patients with sesame, peanut, tree nut, egg, and milk allergies.[25] Thus, it is not surprising that the questions that asked whether children were emotionally impacted by their allergy worsened. Future areas to explore are the roles of patient education in food allergy sequalae, multiple food allergies in QoL, and whether initiation of counseling might further improve emotional well-being and resilience.[13]

Limitations are those associated with retrospective reviews, selection bias, and recall bias. We had a limited single-site patient population, whose patient demographics were not reflective of the diversity of the overall food allergy population. EoE may have been observed in a study with a larger patient population or if our sesame OIT protocol used a screening endoscopy. In addition, the sesame OIT maintenance dose was reduced because the clinical regimen was altered. Furthermore, the diagnosis of sesame allergy without oral challenges may be problematic because there are no clear guidelines or established positive predictive values for skin testing and serum specific IgE levels. During maintenance therapy, although we assessed for the frequency of ARs, the severity of real-world reactions was not quantified. Despite these limitations, analysis of our data showed plausible positive and negative associations between clinical factors and ARs that warrant further exploration.

CONCLUSION

Our study showed a positive correlation between asthma, age, IgE level, and gender, and the risk of ARs, and demonstrated improvements in food anxiety and social limitations. This study helps clarify the relationship between clinical characteristics and ARs during sesame OIT in a U.S. population. Results of our study also suggest a long-term reduced risk of anaphylaxis and food-anxiety due to cross-contamination, which

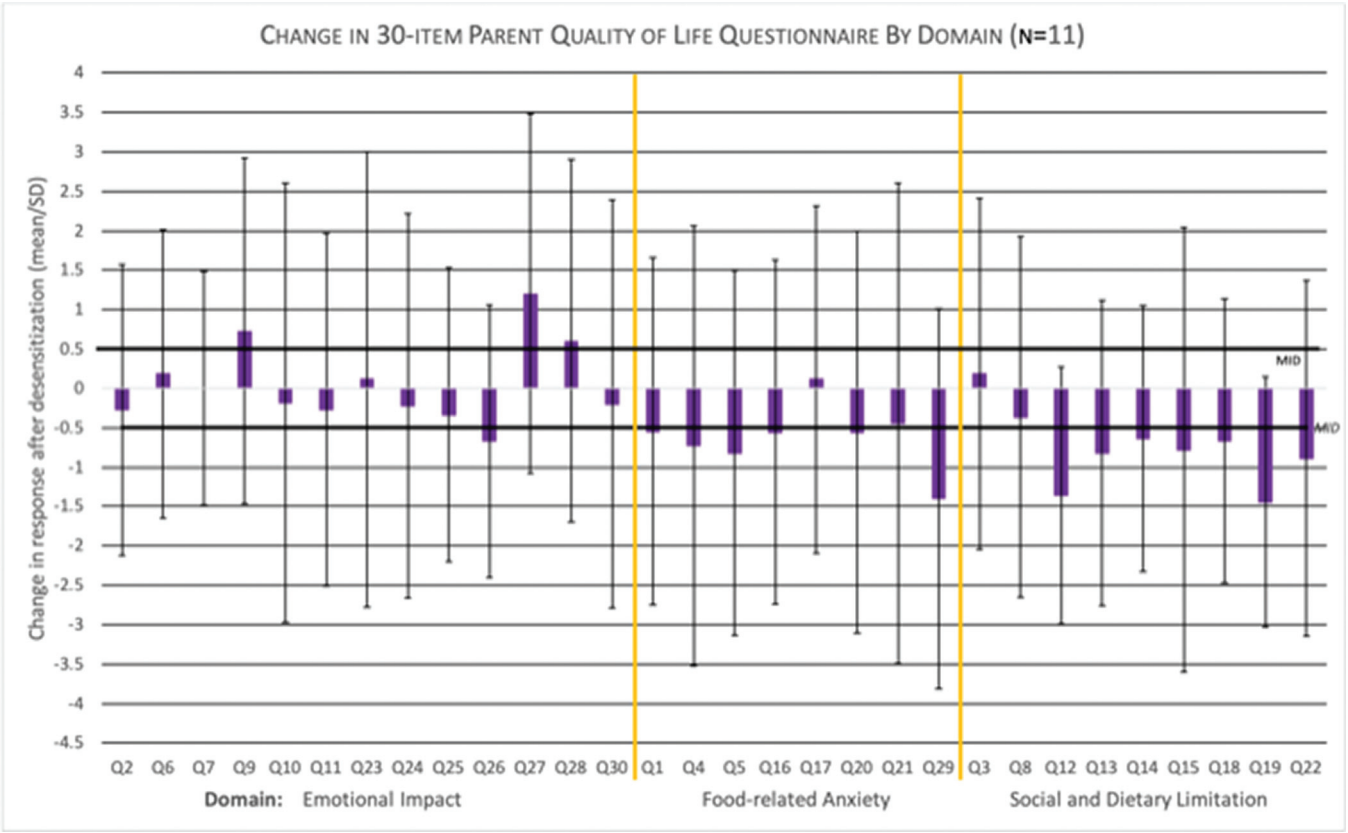

Figure 3. *Quality-of-life analysis for 30-item parent questionnaire by domain. The FAQLQ-parent form post-OIT differed from the FAQLQ-parent form pre-OIT by an additional 20 questions due to revisions by developers. Only the same 30 questions from each survey were compared. The difference in responses is shown by the purple bars with change shown along the y-axis and the question number shown on the x-axis. A positive change indicates worsening, and a negative change indicates improvement. A solid black line at –0.5 demarcates the MID. Gold lines separate each domain. FAQLQ = Food Allergy Quality of Life Questionnaire; OIT = oral immunotherapy; MID = minimally clinically important difference.*

offers patients an alternative to lifelong avoidance and rescue management. As OIT becomes common clinical practice, it is paramount that we continually improve the standard of care and QoL of our patients with food allergy.

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REFERENCES

1. Ram R, Catlin D, Romero J, et al. Sesame: new approaches for crop improvement. Portland, OR: Timber Press; 1990.
2. Warren CM, Chadha AS, Sicherer SM, et al. Prevalence and Severity of Sesame Allergy in the United States. JAMA Netw Open. 2019; 2:e199144.
3. FASTER Act Video for Food Industry and Other Stakeholders: Constituent Update. U.S. Food and Drug Administration. 2022. https://www.fda.gov/food/cfsan-constituent-updates/faster-act-video-food-industry-and-other-stakeholders. Accessed February 4, 2022.
4. Nachshon L, Goldberg MR, Levy MB, et al. Efficacy and safety of sesame oral immunotherapy - a real-world, single-center study. J Allergy Clin Immunol Prac. 2019; 7:2775–2781.e2.
5. Warren CM, Chadha AS, Sicherer SH, et al. Prevalence and severity of sesame allergy in the United States. JAMA Netw Open. 2019; 2:e199144.
6. Blom WM, Michelsen-Huisman AD, van Os-Medendorp H, et al. Accidental food allergy reactions: products and undeclared ingredients. J Allergy Clin Immunol. 2018; 142:865–875.
7. Ziegler JB, Aalberse RC. Sesame: an increasingly popular word and common food allergen. J Allergy Clin Immunol Pract. 2020; 8:1689–1691.
8. Kulis M, Wright BL, Jones SM, et al. Diagnosis, management, and investigational therapies for food allergies. Gastroenterology. 2015; 148:1132–1142.
9. Blackman AC, Anagnostou A. Identification of goals and barriers to treatment from 92 consecutive consultations with families considering peanut oral immunotherapy. Ther Adv Vaccines Immunother. 2019; 7:2515135519869763.
10. Afinogenova Y, Rubin TN, Patel SD, et al. Community private practice clinical experience with peanut oral immunotherapy. J Allergy Clin Immunol Pract. 2020; 8:2727–2735.
11. Factor JM, Mendelson LM, Lee JO, et al. Effect of oral immunotherapy to peanut on food-specific quality of life. Ann Allergy Asthma Immunol. 2012; 109:348–352.e2.

12. Lucendo A, Arias A, Tenias JM. Relation between eosinophilic esophagitis and oral immunotherapy for food allergy: a systematic review with meta-analysis. Ann Allergy Asthma Immunol. 2014; 113:624–629.
13. Wasserman RL, Factor J, Windom HH, et al. An approach to the office-based practice of food oral immunotherapy. J Allergy Clin Immunol Pract. 2021; 9:1826–1838.e8.
14. Epov L, Garkaby J, Almog M, et al. Using skin prick test to sesame paste in the diagnosis of sesame seed allergy. J Allergy Clin Immunol Pract. 2020; 8:1456–1458.
15. Mori F, Barni S, Liccioli G, et al. Oral immunotherapy (OIT): a personalized medicine. Medicina (Kaunas). 2019; 55:684.
16. Flokstra-de Blok BMJ. Food allergy quality of life questionnaires (FAQLQ). In: Encyclopedia of quality of life and well-being research. Michalos AC (Ed). Dordrecht: Springer Netherlands, 2319-2322, 2014.
17. DunnGalvin A, de BlokFlokstra BMJ, Burks AW, et al. Food allergy QoL questionnaire for children aged 0-12 years: content, construct, and cross-cultural validity. Clin Exp Allergy. 2008; 38:977–986.
18. DunnGalvin A, Cullinane C, Daly DA, et al. 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; 40: 476–485.
19. Flokstra-de Blok BMJ, DunnGalvin A, Vlieg-Boerstra BJ, et al. Development and validation of a self-administered food allergy quality of life questionnaire for children. Clin Exp Allergy. 2009; 39:127–137.
20. Flokstra-de Blok BMJ, DunnGalvin A, Vlieg-Boerstra BJ, et al. Development and validation of the self-administered food allergy quality of life questionnaire for adolescents. J Allergy Clin Immunol. 2008; 122:139–144.e1-e2.
21. van der Velde JL, Flokstra-de Blok BMJ, Vlieg-Boerstra BJ, et al. Test-retest reliability of the food allergy quality of the life questionnaires (FAQLQ) for children, adolescents and adults. Qual Life Res. 2009; 18:245–251.
22. van der Velde JL, Flokstra-de Blok BMJ, de Groot H, et al. Food allergy-related quality of life after double-blind, placebo-controlled food challenges in adults, adolescents, and children. J Allergy Clin Immunol. 2012; 130:1136–1143.e2.
23. Jaeschke R, Singer J, Guyatt GH. Measurement of health status. Ascertaining minimal clinically important difference. Control Clin Trials. 1989; 10:407–415.
24. Feuille E, Nowak-Wegrzyn A. Allergen-specific immunotherapies for food allergy. Allergy Asthma Immunol Res. 2018; 10:189–206.
25. Epstein-Rigbi N, Goldberg MR, Levy MB, et al. Quality of life of food-allergic patients before, during, and after oral immunotherapy. J Allergy Clin Immunol Pract. 2019; 7:429–436.e2. □