Brief report

Peanut challenges prior to oral immunotherapy demonstrate high tolerance rates in selected patients

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Background: Peanut oral immunotherapy (pOIT) protocols typically remain below the threshold for reaction during the initial dose escalation (IDE) day. However, some patients may have higher thresholds for reaction or may not have an ongoing peanut allergy.

Objective: We sought to characterize the response to an accelerated initial dose escalation (A-IDE) for qualifying low-risk peanut-allergic patients younger than 4 years in which IDE progressed to a full peanut oral food challenge as tolerated.

Methods: Records of 76 pOIT patients younger than 4 years were reviewed. Those with history of peanut reaction with peanut allergy testing of less than 95% positive predictive value for failed oral food challenge were offered an A-IDE. A-IDE proceeded stepwise until patients refused dosing, any reaction occurred, or they tolerated the challenge (cumulative dose: 4000 mg peanut protein). If the A-IDE was not tolerated, patients completed pOIT.

Results: From April 2022 to February 2024, 16 patients participated in an A-IDE. Eleven (68.8%) tolerated the 4000 mg cumulative dose, demonstrating resolution of their peanut allergy. The remaining had mild symptoms not requiring epinephrine. Mean pOIT starting dose following A-IDE was 450 mg (vs 25 mg in standard pOIT). Maintenance dosing was reached with a mean of 5.2 visits (vs 9.7 in standard pOIT).

Conclusions: Nearly 70% of low-risk patients younger than 4 years with previous diagnosis of peanut allergy tolerated a full peanut serving when initiating pOIT. This indicates the importance of diagnostic peanut challenge to selected patients before initiating OIT. (J Allergy Clin Immunol Global 2025;4:100442.)

Key words: *Food allergy, oral immunotherapy, peanut, oral food challenge*

Abbreviations used
A-IDE: Accelerated initial dose escalation
IDE: Initial dose escalation
OFC: Oral food challenge
OIT: Oral immunotherapy
pOIT: Peanut oral immunotherapy
SPT: Skin prick test

INTRODUCTION

Off-label peanut oral immunotherapy (pOIT) has been shown to be safe and effective in protecting infants and young children with peanut allergy from severe reactions on exposure to peanut via cross-contamination or accidental exposure.[1,2] Recommended pOIT protocols start below the threshold for reaction.[3] Although some pOIT protocols increase initial dose escalation (IDE) doses to the point of reaction or extend the IDE over multiple days, there is typically a maximum dose during IDE, and patients are not cleared of their peanut allergy during this process.[4,5] Other pOIT protocols do not elicit a reaction during the IDE day.[3] However, some peanut-allergic patients may have higher thresholds for reaction or may not have an ongoing peanut allergy, given that oral food challenges (OFCs) are not always performed for every patient before OIT initiation. In this single-center study, we sought to define the proportion of "low-risk" patients younger than 4 years with previously diagnosed peanut allergy who tolerate a full peanut OFC during a pOIT IDE.

RESULTS AND DISCUSSION

A total of 76 patients younger than 4 years who participated in pOIT were included in this study. Patients qualified for an accelerated initial dose escalation (A-IDE) on the basis of (1) clinical history of allergic reaction to peanut without anaphylaxis and (2) peanut sensitization of less than 95% positive predictive value for failed OFC (skin prick test [SPT] wheal diameter <8 mm and peanut serum IgE <5 kU/L).[6] Nineteen patients qualified for an A-IDE, of whom 16 elected to participate (Fig 1, *A*). Parents were given the option for an A-IDE, and 3 patients' parents did not move forward because of associated risks.

Of those who participated in the A-IDE, 68.8% (11 of 16 patients) tolerated a full peanut OFC and were cleared of their peanut allergy ($P = .034$) (Fig 1, *B*). At the time of data collection, 6 of the 11 patients who tolerated the A-IDE had a follow-up appointment in an allergy clinic. All continued to incorporate

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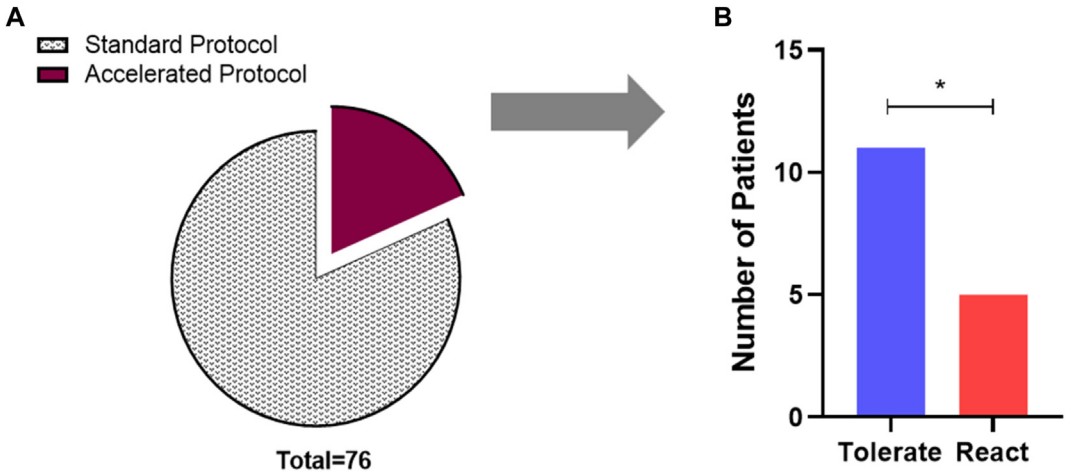

FIG 1. A, Of 76 patients, 16 underwent A-IDE. **B,** Eleven of the 16 patients tolerated peanut OFC, and 5 reacted. *P* values were calculated with 2-sided unpaired *t* tests. $*P \leq .05$.

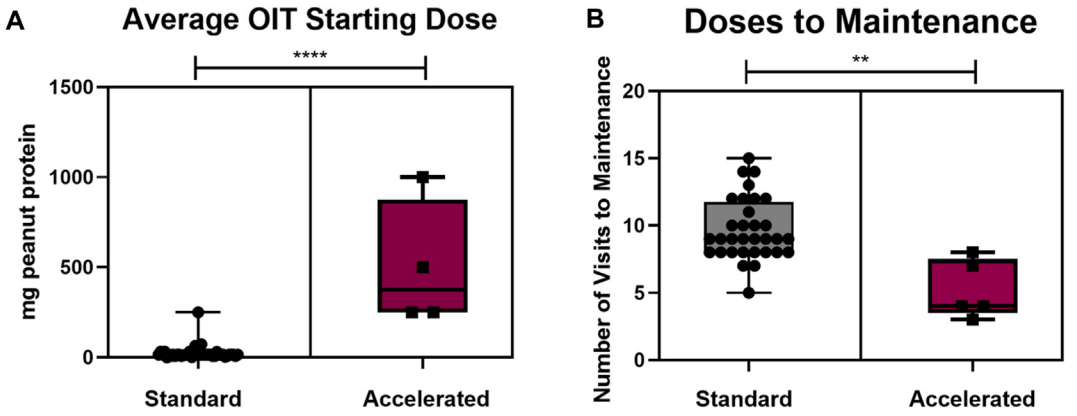

FIG 2. A, Patients who reacted during the A-IDE started pOIT at a higher mean dose than did standard protocol pOIT patients (450 mg vs 25 mg peanut protein). **B,** Standard protocol pOIT patients reached maintenance at a mean of 9.7 visits compared with 5.2 visits for A-IDE patients. *P* values were calculated with 2-sided unpaired *t* tests. $****P \leq .0001$; $***P \leq .001$; $**P \leq .01$; $*P \leq .05$.

peanut into their diet without issue. The 5 patients who reacted during the A-IDE had mild symptoms such as rash, localized hives, and rhinorrhea—all grade 1 reactions on the Consortium for Food Allergy Research grading scale.[7] None required treatment with epinephrine. Patients who reacted during the A-IDE started pOIT at a higher mean dose than did standard protocol pOIT patients (450 mg vs 25 mg peanut protein; $P < .0001$) (Fig 2, *A*). They also reached maintenance dosing with fewer visits (with a mean of 5.2 visits vs 9.7 visits) (Fig 2, *B*).

Of note, there was a male predominance in the group that reacted during A-IDE ($P = .02$). This group was also older at the age of first peanut reaction compared with those who tolerated the A-IDE (with mean ages of 10.2 ± 2.6 months and 7.1 ± 2.2 months, respectively; $P = .03$) (Table I). History of atopic comorbidities was not statistically different between these groups except for allergic rhinitis, which was more prevalent in the group that reacted during the A-IDE. When comparing baseline peanut IgE levels, peanut Ara H2 IgE levels, as well as peanut SPT wheal and flare for those who tolerated their A-IDE and those who did not, there were no statistically significant differences between the groups (Fig 3).

There are limitations to this study. Data were collected from a single center with a small cohort. There is also a lack of racial and ethnic diversity within our pOIT population (Table I). Further multicenter studies with greater sample sizes and diversity are needed to corroborate the results and verify the safety of this protocol.

This study demonstrates that pOIT referrals of low-risk peanut-allergic patients (those without history of anaphylaxis to peanut and low peanut specific testing as described earlier) younger than 4 years are likely to be cleared of their peanut allergy. The implications of a diagnosis of peanut allergy are profound, and it is vital that each patient's diagnosis is accurate. Although peanut anaphylaxis can be life-threatening, inaccurate diagnosis is not benign. Currently available clinical testing for peanut allergy, such as serum IgE levels and SPT, have a varying degree of accuracy, and false-positive food allergy testing results can occur in up to 50% of cases.[8] Therefore, clinical history is arguably the most accurate way to diagnose food allergy, although most initial peanut-allergic reactions do not progress to anaphylaxis.[9] Given the age of patients in this study, clinical history may not be as reliable because of developmental limitations in verbally reporting

TABLE I. Demographic characteristics

Characteristics	Accelerated subjects (n = 16)	Tolerated A-IDE (n = 11)	Reacted A-IDE (n = 5)	*P* value
Sex: male, n (%)	9 (56)	4 (36)	5 (100)	.0151*
Race, n (%)				
African American	5 (31)	4 (36)	1 (20)	.5448
Asian	0 (0)	0 (0)	0 (0)	.9999
White	12 (75)	8 (73)	4 (80)	.7744
Other	0 (0)	0 (0)	0 (0)	.9999
Unknown	0 (0)	0 (0)	0 (0)	.9999
Age (mo) at IDE, mean ± SD	20.3 ± 9.1	19.9 ± 10.8	21.3 ± 4.1	.7855
Age (mo) at first peanut reaction, mean ± SD	8.1 ± 2.7	7.1 ± 2.2	10.2 ± 2.6	.0277*
Time (mo) between initial reaction and A-IDE, mean ± SD	11.5 ± 8.1	11.7 ± 9.7	11.1 ± 2.8	.8909
Ethnicity, n (%)				
Hispanic or Latino	1 (6)	0 (0)	1 (20)	.1432
Not Hispanic or Latino	15 (94)	11 (100)	4 (80)	.1432
Atopic comorbidities, n (%)				
Eczema	14 (88)	10 (91)	4 (80)	.5719
Asthma	4 (25)	2 (18)	2 (40)	.3840
Allergic rhinitis	3 (19)	0 (0)	3 (60)	.0020†
Other food allergies	10 (63)	6 (55)	4 (80)	.8513

*$P \leq .05$.
†$P \leq .01$.

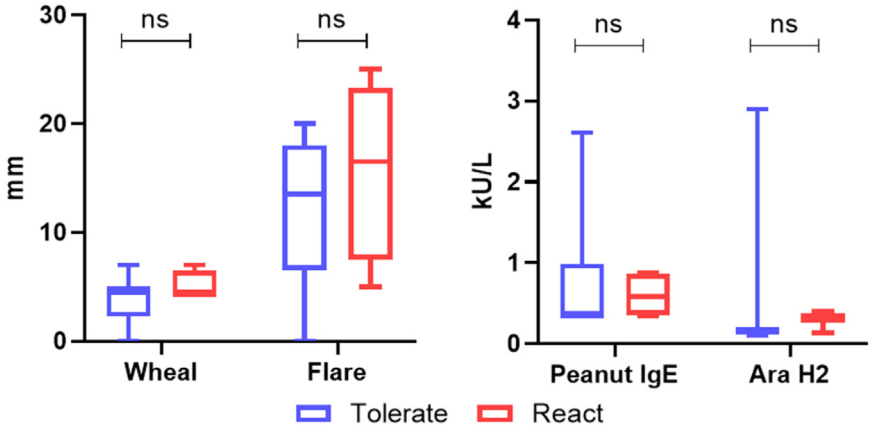

FIG 3. Initial peanut testing results were compared between those who tolerated their A-IDE (*blue*) and those who reacted (*red*). There were no statistically significant differences in initial testing between the groups. *P* values were calculated with 2-sided unpaired *t* tests. To qualify for A-IDE, peanut testing required an SPT wheal diameter of less than or equal to 8 mm and peanut serum IgE value of less than or equal to 5 kU/L. *NS,* Not significant.

symptoms. Thus, an accurate diagnosis before initiating life-long therapy is critical to avoid the "disaster of misdiagnosis."[10]

Food allergies affect relationships, participation in activities, bullying rates, and overall mood, especially anxiety and stress.[11] Financially, food allergies create a burden on families because of the cost of appointments, epinephrine autoinjectors, medications/treatments, emergency department visits, hospitalizations, and specific dietary needs.[12] Delabeling of peanut allergy becomes challenging after pOIT initiation because allergists must then distinguish between peanut desensitization and tolerance. In this study, even those patients who reacted during the A-IDE did not experience severe reactions, and they were able to reach maintenance OIT with fewer visits than standard protocol patients, thus saving families considerable time and expense. There are various approaches to IDE, protocols, and maintenance dosing for pOIT that can extend or reduce commitments for families.[13] Other studies have used the approach of increasing the initial dosing to reaction to reduce time to maintenance dosing.[2,4,5] It is pertinent for providers to evaluate patients for true peanut allergy to reduce potential undue burdens onto families.

Treatment using pOIT has been shown to reduce anxiety and improve quality of life for peanut-allergic patients, but it is recommended as a life-long therapy.[14] This study demonstrates that approximately 70% of low-risk individuals younger than 4 years tolerate a peanut OFC, negating the need for peanut allergy

treatment or continued avoidance. Therefore, before initiating life-long pOIT, the authors recommend consideration of a peanut OFC in low-risk individuals.

DISCLOSURE STATEMENT

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Clinical implications: Low-risk peanut-allergic children as defined by age, clinical history, and allergy testing should be offered a peanut OFC before starting OIT because most of them tolerate peanut.

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