Identification of goals and barriers to treatment from 92 consecutive consultations with families considering peanut oral immunotherapy

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Andrea C. Blackman and Aikaterini Anagnostou

Abstract

Background: Peanut allergy has become an important public health issue. It can be the cause of severe reactions and also the trigger of significant anxiety for the allergic individual, especially with regards to the risk of unintentional accidental exposures. Peanut oral immunotherapy (POIT) is a newly developed treatment approach that has been shown to be highly effective in multiple research studies and has been associated with an acceptable safety profile. This treatment modality is likely to become more mainstream in the next few years with new commercial entities pursuing United States Food and Drug Administration approval for relevant products and multiple providers offering various forms of immunotherapy in their practices.

Methods: The aim of our study was to obtain an accurate assessment of goals of treatment as well as concerns and barriers from families considering POIT in either the research or clinical setting. A single clinician allergist met with all the families and conducted semi-structured interviews on POIT. Families were provided with standardized written information on POIT prior to the consultation, which was used as a formalized instrument to communicate treatment protocols. Conversations were not recorded, but collected information was scribed by a second clinician who did not actively participate in the consultation. Scribed information was coded by the investigators. Thematic analysis identified common topics emerging from the discussions.

Results: We report on the results of 92 consecutive family consultations on POIT conducted over a period of 1 year. Approximately 50% of the families had already researched POIT online, with 25% of families reported being part of Facebook parent groups. Groups identified the following areas as the most important considerations: efficacy, practical information, safety, benefits and goals, eligibility criteria and support in making the right decision. For all families pursuing POIT for their child, the initial goal was achieving protection from accidental exposure and cross-contamination and for approximately one-quarter, consumption of high peanut doses was the ultimate goal.

Conclusion: Our research adds to the limited available data in this area and provides information that may be used as an initial platform for clinical consultations and shared decision-making in POIT. Obtaining a better understanding of patients' expectations and concerns will hopefully facilitate this process, enabling more fruitful and engaging interactions between families and healthcare providers in the field of food allergy.

Keywords: allergy, barriers, children, decision-making, goals, oral immunotherapy, peanut

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Correspondence to:
Aikaterini Anagnostou
Texas Children's Hospital, Department of Pediatrics, Section of Immunology, Allergy and Retrovirology, 1102 Bates Avenue Ste 330, Houston, TX 77030, USA
Aikaterini.Anagnostou@bcm.edu

Andrea C. Blackman
Texas Children's Hospital, Department of Pediatrics, Section of Immunology, Allergy and Retrovirology, Houston, TX, USA

Baylor College of Medicine, Houston, TX, USA

Introduction

Peanut allergy has become an important public health issue with increasing prevalence estimated to affect 1 in 13 children in the United States (US).[1] It can often be severe and runs a lifelong course for the majority of patients, following them into adulthood.[2] Peanut allergy has been associated with life-threatening anaphylaxis and also fatal outcomes and its burden is evident in many aspects of a patient's life, including dietary limitations, social restrictions and psychological impact.[3,4] It can be the trigger of significant anxiety for the individual, especially with regards to the risk of unintentional accidental exposures.[5] Until recently, the only available management option has been strict avoidance of peanut and carriage of emergency medication (epinephrine) to treat any allergic reactions resulting from accidental exposure.[6]

Peanut oral immunotherapy (POIT) is a newly developed treatment approach for patients with peanut allergies that has been shown to be highly effective with an acceptable safety profile in research studies.[7–17] There are a variety of research protocols, but most POIT protocols include an initial escalation phase, a slow up-dosing phase and a long-term maintenance phase. An entry food challenge to peanut (also known as 'baseline challenge'), occurring prior to POIT initiation, may also be required in some, but not all, research studies.

With new commercial entities pursuing US Food and Drug Administration approval for relevant products[18] and multiple providers offering various forms of immunotherapy in their practices, it is important and timely to obtain an accurate assessment of goals of treatment as well as concerns and barriers from families considering POIT. One of the biggest challenges physicians will be facing in the future is optimizing their role in shared decision-making in the context of POIT. Having a better understanding of patients' expectations and concerns will hopefully facilitate this process, enabling more fruitful and engaging interactions between families and healthcare providers in the field, in addition to helping patients make better decisions suited to their needs.

The aim of this research was to evaluate parental expectations, concerns and barriers with regards to POIT in order to facilitate future shared decision-making.

Methods

Patients were recruited from the allergy clinics at Texas Children's Hospital. Specifically, parents of children with peanut allergies who expressed an interest in POIT were offered the opportunity to undergo a separate consultation dedicated to only discussing POIT. Families were offered the option to participate in future research or clinical POIT programs in our institution depending on availability. The consultation was provided on a different day from the initial clinic visit. Families of current ongoing research trial participants were excluded from participation. Children with a diagnosis of eosinophilic esophagitis, underlying immune deficiencies, uncontrolled asthma, severe allergic rhinitis (candidate for allergy shots), uncontrolled spontaneous urticaria and severe atopic dermatitis were also excluded.

A single clinician allergist (AA) met with all the families and conducted semi-structured interviews on POIT. The framework of themes to be explored and the interview guide used were based on existing published data and the aims of the project. Families were provided with standardized written information on POIT prior to the consultation, which was used as a formalized instrument to communicate treatment protocols. All consultations took place in a patient room within the allergy clinic space. Both parents were encouraged to participate, but if one caregiver was not available the consultation took place with the other parent. Conversations were not recorded, but collected information was scribed by a second clinician (ACB) who did not actively participate in the consultation. Scribed information was coded by the investigators. Thematic analysis identified common topics emerging from the discussions.

Approval was obtained from the Baylor College of Medicine Intuitional Review Board (IRB) for prospective collection and storage of clinical data obtained during clinic consultations (IRB protocol H-40400) in the allergy clinic. The consultations were undertaken as part of routine clinical

care, and explicit consent for participation in the consultations was obtained. Individual consent for inclusion in the present study, based on information from the consultations, was waived by the IRB because the research and the use or disclosure of protected health information involved no more than minimal risk (including privacy risks) to the individuals. The information generated from data analysis to be used for research/publication purposes was anonymized so that individuals are not identifiable.

Results

We report on the results of 92 consecutive family consultations on POIT conducted over a period of 1 year (January 2018 to December 2018).

The demographics of our peanut-allergic cohort are shown on Table 1. Briefly, median age at the time of consultation for children with peanut allergies was 8 years old, with a median age of initial adverse reaction to peanut at 1.5 years old. The majority of our patients (78%) had multiple

Table 1. Demographics and characteristics of our patient cohort.

Characteristics and demographics		
Age of cohort (in years)	Median: 8	IQR: 5.75–10
Age at index reaction (in years)	Median: 1.5	IQR: 1–2.25
Recent peanut SPT (measured in mm)*	Median: 14	IQR: 10–20
	***n* = 92**	**%**
Sex		
Male	50	54
Female	42	46
Race and ethnicity		
White non-Hispanic	63	68
Asian non-Hispanic	17	18
White-Hispanic	3	3
Black non-Hispanic	3	3
Asian-Hispanic	1	1
Unrecorded	5	5
Family history of atopy		
Positive	78	85
Negative	13	14
Unrecorded	1	1
Atopic comorbidities		
Allergic rhinitis	78	85
Other food allergies	72	78

(Continued)

Table 1. (Continued)

Characteristics and demographics		
Atopic dermatitis	71	77
Asthma	41	45
Index reaction to peanut		
Positive index reaction to peanut	73	79
Never ingested	19	21
Body systems involved in the index reaction	***n* = 73****	**%**
Cutaneous	43	59
Cutaneous + gastrointestinal	11	15
Cutaneous + respiratory	7	9
Cutaneous + gastrointestinal + respiratory	5	7
Gastrointestinal	5	7
Respiratory	2	3
Treatment received for index reaction to peanut		
Oral antihistamines	53	73
IM epinephrine	8	11
Albuterol	3	4
Oral steroids	4	9

IQR, interquartile range; SPT, .
*Performed within the last 12 months.
**Only patients with a clinical history of reaction to peanut ingestion are included here.

food allergies, with only 22% diagnosed with only peanut allergy. Atopic comorbidities were present in 96%, with allergic rhinitis and atopic dermatitis affecting more than two-thirds and asthma in almost half. Approximately one-fifth of our patients had never ingested peanut previously, but had specific immunoglobulin (Ig)E levels and peanut Skin prick test (SPT) results above the previously established 95% cut-off level (SPT $>$ 8 mm and specific IgE $>$14 kU/l)[19] and had been avoiding peanut completely since diagnosis. Cutaneous symptoms were most commonly reported for the index reaction to peanut, but almost a third reported anaphylaxis on the first exposure.

The average time of each consultation was 60 min with a range of 50–80 min. Typically, both parents were present for most consultations, but if only one parent was present, this was usually the mother. Overall, three consultations occurred with only the father present.

Common topics of discussion that emerged from the consultations following data analysis included the following (see also Table 2):

Table 2. Common sample questions from families considering POIT arising during the consultation and presented by thematic topics.

Common questions from families considering POIT by topic
1. Efficacy:
How successful is POIT?
If my child has a high specific IgE level to peanut, will it be more difficult to achieve desensitization?
Is there a better age to start OIT?
Is there a potential cross-desensitization between peanuts/tree nuts?
2. Practical information:
How long is the whole process going to take?
What is the longest time needed to reach maintenance?
How long does an up-dosing visit last?
Does my child need to have a peanut challenge before POIT?
How often will blood work be done?
How are the daily dosages going to be offered?
What if the daily dosage is skipped or forgotten?
What happens if my child is ill during POIT?
My child takes a daily antihistamine for nasal allergies, is it possible to continue this during POIT?
Is it possible to change the schedule of the daily doses to earlier or later that day if needed?
After the daily dosage of POIT, does my child need to be sitting completely still during the no-exercise period?
Can my child walk to school/ride their bike during the 2-hour observation period?
Is the peanut flour taste unpleasant?
3. Safety:
How safe is POIT?
What is the percentage of reactions during POIT?
What are the most common reactions?
How often does anaphylaxis happen during POIT?
Do reactions happen mostly during up-dosing visits or at home?
What do we do if a reaction happens at home?
If my child stops POIT for some reason, will this make his peanut allergy worse?
How frequent is EoE during POIT?
What is EoE and how is it treated?

(Continued)

Table 2. (Continued)

Common questions from families considering POIT by topic
Have there been any deaths from POIT?
4. Benefits and goals:
Is my child going to be cured from his/her peanut allergy?
Do we still need to carry an epinephrine auto-injector after reaching maintenance?
Does it make a difference being only allergic to peanut or having multiple food allergies?
We want our child to be protected from severe reactions
I want her/him to be able to go to parties without worrying
When he goes to college, I want him to be protected from accidental reactions to peanut
When we reach maintenance, is it possible to proceed to higher doses so peanut can be freely introduced in the diet?
5. Eligibility:
What are the reasons to be declined the option of POIT?
My child is currently in another IT treatment, is he/she eligible for POIT?
If an allergic reaction happens that requires the use of epinephrine, does it mean my child needs to discontinue POIT?
Are children with all levels of specific IgE to peanut included?
Why does my child need to have his/her asthma, allergic rhinitis and eczema controlled before the start?
6. Support:
In your opinion, what is the best decision?
What would you do if she/he was your child?
Is there a number to call if any reactions happen or if I have any questions?
7. Barriers:
Lack of insurance coverage
Time commitment
Daily 2-hour exercise restriction
Personal reasons

EoE, eosinophilic esophagitis; Ig, immunoglobulin; OIT, oral immunotherapy; POIT, peanut oral immunotherapy.

Efficacy

All families requested information about the efficacy ('success rate') of POIT and whether this outcome could be predicted for their own child. Age of the child and levels of specific IgE to peanut as a predictive factor of POIT success were also questioned by some parents. Families with young children were noted to be either more motivated to intervene early in life or less keen to participate due to age-related difficulties (such as compliance with treatment and adherence to exercise restrictions). In cases of children who

were also tree nut allergic, families asked about any potential cross-desensitization effect.

Practical information

Duration of treatment, time to reach maintenance dose, time required for each appointment and number of days missed from school were all common questions. Many families wanted to know whether their child would need to undergo an entry peanut challenge, how often blood work and skin prick testing would be done, how doses were administered, what would happen if a dose is forgotten or missed, whether the peanut dose needs to be given exactly at the same time each day and what food materials could be used as vehicles. Few families asked about the taste of the product and its acceptability. Other queries included what happens if the child becomes ill during POIT and whether regular medication can be administered alongside POIT. A significant number of parents requested clarification on the 2-hour exercise restriction after dosing, especially in terms of what was meant by 'exercise' (i.e. 'Does my child need to be completely still for 2 h?').

Safety

All families raised concerns about safety. There were practical questions on how to proceed if a child has a reaction at home and whether experiencing anaphylaxis results in POIT discontinuation. Parents wanted to know how likely it was for reactions to occur at home, if the same dose was tolerated in the hospital. There were also many questions with regards to frequency and severity of adverse events. Almost all families asked for specific percentages of children experiencing anaphylaxis and requiring epinephrine. Parents also asked if participating was likely to have a negative effect on their child's existing allergy in terms of more severe allergic reactions in subsequent exposures. Some families wanted to know the risk of eosinophilic esophagitis and many of these were not familiar with this disease and requested more information. A few parents asked whether there had been any reported fatalities from POIT.

Benefits and goals of therapy

The overwhelming majority of families voiced an expectation for POIT to provide protection against accidental exposures, especially when the child would be out of the home, for instance, at daycare, school, a restaurant, a party or college. Only a few families showed interest in high-dose POIT with the goal of introducing large doses of peanut in their child's regular diet or *ad libitum* consumption. All families showed a good understanding of the benefits that POIT would confer to their child.

Eligibility criteria

Parents were often concerned that their child may not be eligible for POIT and asked for any contraindications to participating in this treatment. Families also inquired about specific IgE cutoffs used as an eligibility criterion and whether undertaking a different form of immunotherapy (e.g. allergy shots) excluded their child from participation. None of the families were aware that uncontrolled asthma is a contraindication to POIT.

Support

Most families expressed a desire for help in making the right decision for their child. This referred not only to the decision of undertaking POIT or not, but also to the identification of the 'right time for this'. Approximately two-thirds of the families requested the physician's personal opinion on whether their child should undergo this treatment. Approximately 50% of the families had already researched POIT online, with 25% of families reported being part of Facebook parent groups, which were posting POIT experiences and offering advice to interested individuals.

Barriers

Following this initial consultation, 86% of families reported no barriers to POIT participation. A small number of families (14%) reported the following barriers: potential lack of insurance coverage and inability to pay for this treatment, inability to make the necessary time commitment, inability to adhere to the daily 2-hour exercise restriction and personal reasons.

Discussion

To our knowledge this is the first study that evaluated parental expectations, concerns and barriers of families who are considering POIT

treatment for their child. We were interested in patients' views and understanding of this treatment, with the aim to facilitate future shared decision-making, especially considering the burgeoning demand for POIT.

One of our first observations was that consulting patients on POIT required a significant amount of the clinician's time, with most consultations lasting an average of 60 min. The decision on whether to undertake POIT or not is complex and multiple factors need to be considered. In order to provide the relevant information, evaluate the family's baseline knowledge on POIT, discuss any concerns and address all their questions, dedicated time is needed.

We noted that practical information with regards to the process of POIT was important for families, with time commitment (both short-term and long-term) being the most discussed topic. All individuals appreciated the time required and realized that POIT is a long-term process rather than a 'quick fix' solution. Our handout sheet provided the information that POIT is a long-term commitment, which may explain why parents did not question this fact during the consultation. However, incorporating this into the daily life of families required a detailed discussion of practicalities, taking into account family needs and commitments.

For the large majority of families pursuing POIT for their child, the main goal was achieving protection from accidental exposure and cross-contamination. We identified significant anxiety associated with 'hidden ingredients' in various food products and potential for inadvertent exposure to peanut. This was also associated with an almost overwhelming desire for the child to be safe outside the home environment and to be able to participate in a variety of social activities without fear. Very few families brought up concerns about fatalities, but most were worried about severe reactions occurring as a result of unintentional exposure to peanut. It has been reported previously that parents with higher anxiety about negative outcomes from accidental ingestion may be more likely to participate in food allergy immunotherapy trials.[20]

For approximately one-quarter of families, consumption of high peanut doses was the ultimate goal (the primary goal was still protection from inadvertent exposure). It was mentioned that in these households, peanut was a much-loved food that other nonallergic family members wished to consume without worrying that they would put the allergic child at risk. Cultural reasons (peanut being a key component of the preferred cuisine) and nutritional benefits of nuts were also offered as reasons for pursuing increased consumption. A few families with children with multiple allergies wished for fewer food restrictions and communicated to us that expanding the diet even a little would make a significant difference to their child's limited food choices. We found all this information very interesting especially since a lot of research has focused on examining sustained unresponsiveness to peanut. For many allergists, a cure for peanut allergy is highly desirable, however, it appears that for patients with peanut allergies and their families, a more modest goal of achieving protection from accidental exposures and severe reactions may be equally desired and will likely make a significant difference to their daily quality of life.

Interestingly, our patients' reported goals align with the goals of peanut immunotherapy research participants. A recent publication, which included 6 oral immunotherapy and 12 Epicutaneous immunotherapy research trial participants reported that families participating in food immunotherapy trials express the wish that these treatments would result in their children developing a buffer against accidental peanut exposure. This buffer would increase their confidence in travel and dining outside the home, but would not lessen their overall allergen-associated vigilance and avoidance practices.[21]

As expected, safety, including potential side effects of POIT was a universal topic of discussion. All caregivers wanted to know whether their child would be likely to suffer from any severe or irreversible side effects during treatment. Interestingly, almost all families were willing to take the risk of treatment-related allergic reactions, when this was balanced with the long-term outcome of achieving protection against accidental exposures. Many families asked about entry food challenges and commented that they hoped these would not be necessary prior to starting treatment. There was also a reluctance for frequent blood work undertaken during POIT, with patients (mostly of younger age) unwilling to

participate if this meant that regular blood tests would be required. This view was sometimes reflected on the parents' preferences also, but not consistently.

We identified some unexpected knowledge gaps during our consultations. Very few families considered uncontrolled asthma or any other comorbidity a risk factor for reactions during POIT and needed to be educated on these. There was also limited knowledge on eosinophilic esophagitis in terms of disease presentation and symptoms, highlighting the fact that few families are aware of this disease. We were also slightly surprised that the exercise limitation often required clarification; all parents understood that playing sports was not advised, but for many, a brisk walk or a short cycle ride to school did not qualify as 'exercise'.

Some interesting observations on our part included the fact that neither time for appointments, nor long-term commitment were reported as barriers. Many viewed this treatment modality as a long-term process and were happy to wait in order to achieve their desired goal. Flexibility in the timing of doses was highlighted as important by families in order to avoid interruptions in daily life (holidays, special events), but few reported concerns about adherence to treatment and potentially forgetting or missing doses. Considering that compliance is critical for both the safety and success of POIT, we found this to be an interesting statement and suspect that it may be related to the fact that families wishing to participate in POIT are generally highly motivated. However, another explanation may be that the amount of insight patients have as to the burden of POIT is limited and families are not able to appreciate challenges that arise during POIT prior to actual participation. This lack of insight could also explain the unexpectedly high number (86%) of families who did not identify any barriers to participation. Both observations clearly highlight a significant need for continuous support during POIT in order to complete the initial treatment period and subsequently adhere to long-term dosing requirements. As a first step, we would propose not only having dedicated appointments for POIT discussion, but also potentially hiring trained nurse educators and pediatric psychologists to facilitate decision-making and compliance. In addition, creating resources for families that address common questions arising before, during and after POIT treatment would likely be beneficial and helpful to participants.

Families with young children were noted to be either more motivated to intervene early or less keen to participate due to age-related difficulties. Having multiple food allergies did not appear to be a barrier for families; most of our patients who expressed interest in POIT suffered from more than one food allergy. Surprisingly, very few individuals asked about cost. The reasons for this may have been the assumption that costs would be absorbed by the research trial sponsor, that health insurance would cover the cost of treatment or that this may be a later consideration when POIT participation becomes more imminent.

We did not expect as many patients seeking the physician's own opinion or gathering so much information from online resources (Google, Facebook groups). The first highlights the importance of training in shared decision-making as the clinician is a key facilitator in this process. The second is concerning in terms of unregulated sources of information and nonmedically trained individuals providing medical advice. Both actions however show a clear and real need for support in the decision-making process, which should not be underestimated.

The strengths of our study include the large number of consultations, information gathered from families who were considering POIT, but had not participated in any research trials at the time of the consultation, all discussions undertaken by a single clinician (ensuring consistency in consultations) and information gathered and recorded in a systematic and prospective way.

The limitations include patients from a single center, patients with interest in POIT (potentially more motivated than a general cohort) and a population of patients derived from a tertiary pediatric center that may not be representative of the entire spectrum of children with peanut allergies in the community setting. In addition, we provided information for parents considering POIT in both the research and clinical setting without examining potential differences in populations between the two settings.

In summary, we identified that the following areas were the most important considerations of

families debating POIT: efficacy, practical information, safety, benefits and goals, eligibility criteria and support in making the right decision. Our research provides information that may be used as an initial platform for clinical consultations and shared decision-making in POIT. Insights into the patients' concerns, expectations and goals for therapy, as well as the need for specific information and support will facilitate the physician–patient interaction and ultimately the decision-making process. It is important to highlight that dedicated time is required for POIT discussions and actively listening to patients is a key component of patient-centered healthcare. Multidisciplinary support and patient resources would probably offer families a better insight into the challenges of POIT and provide a necessary support system during the long-term process.

In conclusion, when clinicians and patients work together to make decisions about POIT, it is important to understand where the patient is coming from and what they wish to gain from the consultation. In many situations, there is no right or wrong decision, but a number of choices that affect each patient and family differently. It is therefore essential to present options in an informative, but unbiased way. It is equally important to balance risks and expected outcomes of POIT with patient preferences and values in order to reach the right treatment decision for patients and their families.

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Conflict of interest statement

Dr Anagnostou is Principal Investigator for Aimmune Therapeutics phase III trials of peanut oral immunotherapy. Dr Blackman reports no conflicts of interest.

ORCID iD

Aikaterini Anagnostou https://orcid.org/0000-0001-6240-7437

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