Optimal patient selection for oral immunotherapy

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ABSTRACT

Standard criteria for ideal patient selection with food oral immunotherapy (OIT) have yet to be determined. Although there are a handful of contraindications to consider before recommending OIT, most patients with confirmed immunoglobulin E–mediated food allergies are appropriate candidates. Success rates of OIT can vary widely and be influenced by several factors. Choosing the most appropriate candidate for an OIT program can mitigate risks and provide the best chance for patients to be successful.

(J Food Allergy 4:49–52, 2022; doi: 10.2500/jfa.2022.4.210013)

TAKING BACK CONTROL

Whether it is improved quality of life, increased peace of mind, or protection against accidental exposure, there are a multitude of reasons why patients might choose to seek out oral immunotherapy (OIT) as a treatment option. Whatever their rationalization, the common thread that connects all these patients is their desire to take back control of their lives. Before having OIT as a treatment option, most patients with food allergy had always been on the defensive, maintaining constant vigilance in a world that was unpredictable and unsafe. The only help that allergists seemed to offer was a yearly renewal of an epinephrine autoinjector and the sage advice of strict avoidance. When OIT first became available approximately a decade ago, it was not surprising that many patients with food allergy embraced the chance of changing this dynamic. Some viewed desensitization as the first opportunity to flip the script and finally go on the offensive. Parents of children with food allergy, however, have the opposite problem. Instead of trying to take back control, they are looking for ways to safely give some of that control up. One of the biggest fears that parents face is not being able to manage their child's environment when they leave the house. This includes any situation in which they are not directly involved in the preparation of meals. Whether it is a restaurant, a sleepover, or a college cafeteria, parents have trouble trusting anyone not familiar with the severity of their child's food allergy to provide them a safe meal. As a result, many parents attempt to influence every aspect in their child's life in a well-intentioned attempt to keep them protected. Although this level of control often prevents accidental exposures, it can unknowingly lead to increased childhood anxiety and isolation from normal peer interactions.[1,2] For many parents who deal with these crippling anxieties, OIT provides an outlet to give up some of that control and give their children the freedom to make mistakes and live their lives with more autonomy.[3]

PATIENT-CENTERED CARE AND SHARED DECISION-MAKING

With OIT, allergists can finally offer something other than just strict avoidance, an epinephrine autoinjector, and a written anaphylaxis action plan. However, just because allergists have a new tool for treating food allergies does not mean that it should be used in every case. In fact, not all patients who come in for a food OIT consultation are willing participants. For many, especially adolescents, maintaining the *status quo* is preferable to the rigors that OIT treatment demands, including daily dosing and frequent office visits. Oftentimes, parents and their children are on opposing sides of the treatment paradigm, which can lead to resentment and problems with long-term compliance. Although many parents are desperate to find an answer for their child's condition, it is important to remember that the best outcomes in OIT come when the discussion is focused on patient-centered care and shared decision-making.[4] When a young patient is brought into the fold of the discussion, he or she feels like an active participant in his or her health care rather

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No external funding sources reported

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*This manuscript is part of the **Journal of Food Allergy** collection of published works referred to as the "Oral Immunotherapy Manual." The contents of this work reflects the opinion(s) of the author(s) and is not intended to replace published guidelines or the clinician's medical advice in the doctor-patient relationship*

than as a passive observer. This concept was considered important enough to include in the most recent Canadian Society of Allergy and Clinical Immunology guidelines for OIT, which stated, "the ultimate goal of food allergy care should be the empowerment of patients and their caregivers to manage the risk of food allergy reactions, reduce food-related anxiety, and achieve a sense of control over their condition."[5]

OPTIMIZING PATIENT SELECTION

Because not all patients are good candidates for OIT, it is important to have a better understanding of which patients have the best chance to safely and successfully complete OIT. First and foremost, there needs to be confirmation of an immunoglobulin E (IgE) mediated food allergy before any OIT program can begin. This can be accomplished through a comprehensive clinical history followed by skin-prick testing or serum specific IgE (sIgE) testing if indicated. A substantial number of patients coming in for OIT consultations might not be truly allergic and putting patients through months of unnecessary office visits and daily food ingestion should be avoided. Oral food challenge is required if there is any doubt with regard to the diagnosis or if the clinician wants to establish a baseline threshold before therapy.[6,7] Once a food allergy diagnosis has been established, the next step is to determine who would be a good OIT candidate. OIT is especially effective for those patients with evidence of an IgE-mediated food allergy in whom avoidance measures are ineffective, are undesirable, or cause severe limitations to a patient's quality of life.[8] Patients who experience severe anxiety from food avoidance, cross-contamination exposure, or a previous systemic reaction would benefit from OIT. Parents with toddlers who are close to school age often seek out OIT to help mitigate risks before enrolling them in school. Similarly, parents of adolescents who are close to graduating high school look to OIT to provide a sense of security before moving on to college. Anyone who has failed a recent OFC or has high or unchanged serum sIgE levels and/or skin-prick test wheals over several years can also be considered.

There are several risk factors to consider before starting OIT.[9] Interestingly skin-prick testing and serum sIgE levels do not seem to correlate with the severity of a reaction after exposure and, therefore, should not be used to risk stratify patients with OIT.[10] One risk factor that seems to garner a lot of questions is age. What age is too early to start OIT, and, conversely, what age is too late? There definitely seems to be a correlation between increasing age and diminishing returns when it comes to OIT treatment. Older patients tend to have more adverse effects, especially gastrointestinal, which makes it more difficult for them to complete therapy.[11] Determining the appropriate starting age for OIT cannot be standardized but rather depends on the individual patient, his or her parents, and the food being considered. In the past, some OIT programs restricted starting ages to 3 or even 5 years of age, depending on the patient's maturity, ability to communicate, and capacity to follow directions. With more experience, these restrictions are likely unnecessary, especially because there is growing evidence that starting OIT in younger ages may be associated with better outcomes and fewer systemic reactions.[12–15] In some cases, successful peanut OIT has been reported in children $\leq$12 months of age with some allergists starting OIT soon after a failed infant peanut introduction.[12] In addition, the natural history of food allergy resolution can differ, depending on the food, and should be balanced when determining if a patient is a good candidate for OIT. This is especially important when starting milk or egg OIT at younger ages, given that most of these patients will naturally develop tolerance over time.

Patients with multiple food allergies present another scenario that is challenging because the benefits of single-allergen OIT might not be as apparent in this population.[16] Although there are minimal differences in effectiveness and safety when comparing single-food OIT with multi-food OIT,[17] these patients require ingestion of larger volumes of food daily, which makes long-term compliance more challenging. Furthermore, not all these patients can complete OIT for every one of their food allergies, which limits the benefits enjoyed by those on single-food OIT. Although multiple food allergies are not a contraindication to OIT, these patients might not achieve the same quality-of-life improvements that individuals who are monosensitized experience.

ABSOLUTE AND RELATIVE CONTRAINDICATIONS

Everyone involved in the OIT process must be fully informed of the risks and benefits of therapy. Having a clear understanding of all treatment options currently available as well as any possible future therapies being investigated will allow families to make the most informed decision possible. Providing a comprehensive overview of the OIT program, including clear treatment goals, prevents unrealistic expectations about the benefits of OIT and avoids an overestimation of its risks.[5,18] Proficiency in communication by using simple language and by fostering a discussion on all these important topics is essential to ensure universal understanding.

In our institution, severe, poorly controlled asthma, pregnancy, and poor adherence are absolute contraindications for OIT, and these patients should not be considered for OIT under any circumstances (Table 1). In mirroring previously published safety guidelines for subcutaneous immunotherapy,[19] our practice

Table 1 **Absolute vs relative contraindications for oral immunotherapy**

Absolute contraindications
Severe, poorly controlled asthma
Pregnancy
Poor adherence
Relative contraindications
Preexisting eosinophilic esophagitis
Active severe atopic dermatitis
Chronic urticaria
Cardiovascular disease
Mastocytosis
Use of β-blockers or angiotensin-converting enzyme inhibitors
Lack of commitment from the patient or other psychosocial barriers

continues OIT on patients who become pregnant while on therapy and avoid any dose increases until after delivery. If the patient or family has a history of poor medication compliance with other chronic disease states, *e.g.,* asthma, OIT might not be the best fit. Similarly, if a patient is found to be noncompliant while on OIT, then serious consideration should be given to discontinuing treatment. Life-threatening systemic reactions that require vasopressor support or intubation do not necessarily exclude a patient from considering OIT, although this history may be associated with more adverse effects and dissuade some offices from offering therapy to these patients.

Relative contraindications for OIT include preexisting eosinophilic esophagitis, active severe atopic dermatitis or chronic urticaria, cardiovascular diseases, mastocytosis, or the concomitant use of medications such as β-blockers or angiotensin-converting enzyme inhibitors.[5,7,8] Underlying atopic conditions such as asthma, allergic rhinitis, and atopic dermatitis must be controlled before starting OIT and proactively managed throughout therapy. A patient and caregiver with unhealthy psychosocial dynamics can sometimes jeopardize the safety of OIT and can include but are not limited to unreliable adherence, severe anxiety, psychiatric barriers, noncollaborative family dynamics, a lack of schedule flexibility for proper dosing, and a lack of commitment from patients or caregivers.[5] Recognizing these destructive patterns can be challenging, especially because they do not become apparent until well into treatment. Other obstacles to successful OIT treatment include reluctance to use epinephrine and language barriers, which should be addressed as well if applicable. A decision to pursue OIT in these at-risk patient populations should be based on clinical judgment, provider expertise, and shared decision-making. All the above-mentioned factors need to be considered and discussed with the patient and family in detail before informed consent can be provided.

TEMPERING UNREALISTIC EXPECTATIONS

OIT is a substantial time, financial, and emotional commitment that requires highly motivated families who are ready to put in the work necessary to successfully complete the program. As a result, families should be given an estimation of the time commitment required to reach maintenance as well as the understanding that this therapy could continue indefinitely. Parents and patients oftentimes have unrealistic expectations of what OIT can accomplish, including curing food allergy or allowing for unrestricting eating. Parents, for example, are often excited that their child will be eating lots of peanut butter and jelly sandwiches once peanut OIT treatment is completed. Although free eating can be a goal for some patients, most detest the taste of the food they are allergic to and have difficulty tolerating their daily maintenance dose. Another assumption is that OIT therapy will reduce the risk for systemic reactions. Although it is true that patients who complete OIT have a higher threshold for reaction when exposed to their food allergy, there is a substantially greater risk for anaphylaxis and other allergic reactions when OIT treatment is compared with placebo or food avoidance.[20,21]

CONCLUSION

The main criteria for acceptance into an OIT program include patients and caregivers who are motivated and have a good grasp of the goals and expectations of treatment. Patients do not necessarily have to be excluded based on age, a high baseline food sIgE level, or a history of anaphylaxis. Response to OIT can vary, depending on the patient, the food allergen, and underlying comorbidities, which makes it difficult to predict outcomes or to strictly standardize protocols. Consequently, OIT should be approached as an individualized treatment plan that caters to the patients' evolving needs, which may change throughout the course of therapy. Periodically reassessing patients' goals and perceived benefits, therefore, is required to ensure that clinical decisions continue to reflect personal objectives.[5] This requires patience, creativity, and flexibility on behalf of the care provider, patient, and family. In doing so, caregivers can provide the best chance for patients and their families to achieve their goals for OIT.

CLINICAL PEARLS

- Patients with confirmed IgE-mediated food allergy in whom avoidance measures are ineffective or

undesirable, or cause severe limitations to a patient's quality of life are excellent candidates for OIT.
- Severe, poorly controlled asthma, pregnancy, and poor adherence are absolute contraindications for OIT.
- OIT is a substantial time, financial, and emotional commitment that requires families who are highly motivated and who are ready to put in the work necessary to successfully complete the program.

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