

Is It Time to Offer Peanut Oral Immunotherapy to Toddlers?



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In the era of rising peanut allergy, many efforts have been made to prevent or cure peanut allergy. Approximately 8% of children in the United States have any food allergy, and approximately 2% of all children are allergic to peanut.¹ Peanut allergy accounts for the greatest number of fatalities due to food allergy.² Food allergy is associated with diminished patient and parent health-related quality of life including increased food anxiety, social limitations, and emotional distress.³ Lower eliciting doses for peanut are directly associated with lower health-related quality of life, likely due to the greater risk for reactions due to accidental ingestions.³

The current standard of care for treatment of peanut allergy at any age is to recommend strict dietary avoidance and educate patients and their families on how to treat an allergic reaction should an accidental exposure occur. The preschool age group, however, is arguably difficult to control in regard to these accidental ingestions, given their activity level and developmental curiosity. In more recent years, peanut oral immunotherapy (POIT) has emerged as an additional treatment for peanut allergy. POIT can provide protection against severe allergic reactions during accidental ingestions. Palforzia is the only FDA-approved POIT product available in the United States for patients 4 to 17 years old. Younger patients do not have an FDA-approved peanut immunotherapy option available to them at this time. However, the toddler/preschool years are formative, because the natural course of food allergy may be more pliable and children develop eating habits that may persist into adulthood. One common reason for withdrawal from POIT in older children is the fear and an aversion to the food after being taught to avoid it their whole lives.⁴ By initiating POIT earlier, this aversion may possibly be avoided.

In this issue of *JACI: In Practice*, Soller et al⁵ address the efficacy of POIT in children aged 9 to 70 months in the article entitled “First real-world effectiveness analysis of preschool peanut oral immunotherapy.” The purpose of the study was to evaluate the success of desensitization after reaching 1 year of maintenance dosing of POIT. Children aged 9 to 70 months were recruited from both academic and community allergy clinics. Reaction histories were based on a graded scale from grade 1 (mild), grades 2 and 3 (moderate), and grades 4 and 5 (severe).⁶ Children had to have an objective history of reaction to peanut during an optional baseline oral food challenge (OFC) to a cumulative dose of <300 mg of peanut protein and evidence of sensitization. Baseline oral challenges to confirm clinical allergy were performed when possible based on available resources in this real-world setting, but only performed on 27% of the 161 eligible patients. Alternatively, if there was no baseline OFC, at least 1 objective reaction to dosing during buildup was required, in addition to evidence of any peanut sensitization for those with grade 2 (or higher) reaction history OR skin prick test ≥ 7 mm and specific IgE ≥ 2 kU/L for those with only grade 1 reaction history or no peanut ingestion history at all. These stringent criteria ensure that the patients included in the study have true clinical allergy to peanut. Patients underwent POIT protocols using either peanut flour, Bamba, or both as published in their previous study, which demonstrated the safety of these protocols,⁶ and symptoms were graded systematically. After patients were on the maintenance dose of 300 mg for 12 months, they were invited for an open peanut OFC with a cumulative dose of 4000 mg of peanut protein. The primary outcome comprised tolerance of the cumulative dose of 4000 mg, and a secondary outcome was the proportion of patients tolerating a cumulative dose of 1000 mg of peanut protein. POIT was started on 185 eligible preschoolers; 24 dropped out during buildup or maintenance, and 161 were eligible for and 117 underwent the OFC. The 4000 mg cumulative dose was tolerated without symptoms in 78.6% of the preschoolers, and 98.3% were able to tolerate ≥ 1000 mg cumulative dose. Of the patients with a positive OFC, 2 (1.7%) were treated with epinephrine and 1 was transferred to the emergency department. In an intention-to-treat (ITT) analysis, the authors found that POIT was 57% effective at reaching the cumulative 4000 mg of peanut protein, assuming that the 44 who did not receive the follow-up OFC would have reacted.

This study⁵ highlights the effectiveness of POIT in the preschool age group, in which over 98% of children tolerated at least 1000 mg of peanut protein and 78.6% were able to tolerate 4000 mg of peanut protein, which suggests significant protection against accidental ingestions in both groups.⁷ Findings are similar to a previous study, which took the outcome a step further and demonstrated sustained unresponsiveness with a 5000 mg peanut

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protein challenge 4 weeks after stopping POIT in 85% of preschoolers on a 300 mg maintenance dose and in 76% of preschoolers on a 3000 mg maintenance dose in an ITT analysis.⁸ These 2 studies^{5,8} show a higher efficacy of POIT in preschool-aged children as compared with older children, among whom only 67% tolerated 600 mg and 50.3% tolerated 1000 mg of peanut protein after POIT with a 300 mg maintenance dose (ITT analysis).⁹ This supports the notion that peanut allergy may be less established at this early age and the early childhood years may be crucial for changing the allergy trajectory. There were also more adverse events in POIT among older children with 87.1% of participants experiencing an adverse event in the 4- to 17-year age group⁵ compared with the 10.5% of preschool children who had reactions during maintenance in this study on the same 300 mg maintenance dose.⁵ A strength of this study is the applicability to the real-world setting as POIT was performed in community allergy clinics for almost 90% of the patients. This is highly relevant as many patients with peanut allergy do not have access to an academic center. Even with the ITT analysis including patients who did not receive the follow-up OFC, POIT was effective in the majority of children aged 9 to 70 months. Furthermore, the strict inclusion criteria create a reasonable likelihood of true clinical allergy in the majority of patients. Not all patients in the study had baseline OFCs, which mimics real-world allergy practice where clinical allergy is often diagnosed based on a history of objective reaction and evidence of sensitization, as baseline OFCs can be risky endeavors that parents may not be willing to pursue. One limitation of the study is that sustained unresponsiveness was not evaluated and another one is that the study procedures were not blinded. However, the authors hypothesize that after a decade of peanut OIT starting in these early ages, sustained unresponsiveness may be tested in real life during the adolescent years when compliance for oral immunotherapy wanes.

The preschool years are a unique time when parents have significant control of the child's diet and feeding habits are formed. As the authors have demonstrated, this is an ideal time to start POIT.

This study highlights the need for peanut immunotherapy options in the preschool age group. By waiting to initiate POIT until school-age or teenage years, we may be missing a critical window of opportunity for well-tolerated and effective POIT that can change the allergic trajectory for the lifetime. Furthermore, early introduction of peanut-containing food is recommended for at-risk infants, but often missed in those considered likely allergic due to a large peanut SPT or specific IgE in the absence of a history of peanut ingestion. These patients may be ideal candidates for POIT, and this intervention may help prevent development of clinical peanut allergy or change its natural history. Expanding POIT to include the preschool age group paves the way for a more active role of an allergist in the prevention and management of peanut allergy.

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