



Peanut allergy reduction in high-risk pediatric patients

Abstract: *The prevalence of food allergies has doubled in the past 10 years. Peanut allergies are a significant public health issue and are the primary reason for food-related anaphylactic reactions that result in death. Evidence supports that early introduction of the peanut protein (or in combination with immunotherapy) to the highly allergic may safely desensitize patients, which could lead to less adverse allergic reactions and alter allergy management overall.*

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The prevalence of food allergies has doubled in the past 10 years.¹ In primary care, providers are regularly seeing more patients with significant food allergies. These patients may present with the following mild symptoms: a runny nose, rash, urticaria, edema, pruritus, a tingling sensation in the throat or mouth, and gastrointestinal issues such as diarrhea, abdominal cramping, nausea, and vomiting.² Some patients may have more severe symptoms, even on their first reaction, such as facial edema, choking or breathing difficulty, wheezing, or even anaphylaxis.³

Children are the most prone to food allergies, with a peak age of onset at 18 months.¹ In the year 2000, the American Academy of Pediatrics (AAP) recommended the elimination of foods that children were allergic to or had been deemed allergic via testing.⁴ In 2008, the AAP reviewed the guidelines, and there was not enough evidence shown requiring the current guideline to be changed.⁴ Nuts, soy, wheat, eggs, and milk are the most common food allergies.⁵ Children who are allergic to peanut products typically react after their initial exposure. Adults have the same common allergens as children,

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but this list also includes shellfish, fish, fruits, and vegetables.⁶

As the primary reason for food-related anaphylactic reactions that result in death, peanut allergies pose a significant public health issue.¹ It is imperative to identify preventive strategies for those with peanut allergies given the severity of the potential reactions, such as anaphylaxis. Children who are deemed high risk for peanut allergies include those who have other known food allergies, asthma, or atopic dermatitis. High-risk children can also include those who have siblings or parents with a known peanut allergy.

The AAP previously made recommendations to avoid peanuts in high-risk children until age 3.⁴ The AAP endorsed the most current guidelines, *Addendum guidelines for the prevention of peanut allergy in the United States: Report of the National Institute of Allergy and Infectious Diseases—sponsored expert panel*.⁷ The guidelines utilize a three-tiered exposure level. The first level, considered as high-risk infants, applies to infants with severe eczema, egg allergy, or both. The recommendation is to initiate peanut exposure at approximately 4 to 6 months of age. Allergy testing is advised but not mandated in this group. Level two, infants with mild-to-moderate eczema, should be introduced to peanuts at 6 months of age. Level three includes infants without eczema or food allergy who are not at increased risk for peanut allergy, and those children can be introduced when solid foods are introduced per parental preference.⁷

According to Roy and Roberts, it is thought that U.S. rates for peanut allergies (and other nuts) are between 1.6% and 2.7%.⁸ Although there are some theories regarding the apparent increase in the prevalence of food allergies—especially peanut allergies—there is a lack of good evidence on how to prevent them from occurring. Additionally, oral immunotherapy seems promising as an avenue for desensitization.⁹

This article provides a guide to further investigate if early peanut introduction, rather than delayed introduction, is related to the incidence of peanut allergies and will review if oral immunotherapy can be used for desensitizing high-risk children as well as children who have already been diagnosed with a peanut allergy.

■ Infants at risk for peanut allergy

In 2015, the *New England Journal of Medicine* published the results of the Learning Early About Peanut Allergy (LEAP) trial, which was conducted by Du Toit

and colleagues.¹ This trial concluded that when there is an introduction of peanuts earlier in childhood, the prevalence of peanut allergies in children who are at high risk of having these allergies is reduced.¹ Du Toit and colleagues examined the early introduction of peanuts in children who were deemed more likely to develop peanut allergies over a period of 5 years. The LEAP trial included 640 children who had skin-prick testing to assess the risk of a significant allergy. At the onset of the trial, participants were between the ages of 4 and 11 months, and 98 of the subjects had a positive allergy skin test result.

At age 5 years, Du Toit and colleagues reevaluated the 98 children with positive skin tests who were divided into a consumption and avoidance group. The researchers found that less than 11% of the group that consumed peanuts was found to be allergic versus more than 35% of the avoidance group. A group of 530 infants who initially had a negative skin allergy test were given a specific amount of peanut protein over a period of 5 years, with each amount increasing in measurement. At age 5 years, the results showed that 13.7% of the avoidance group tested positive for active peanut allergy, and less than 2% showed a peanut allergy in the consumption group of children. These results show a compelling reduction in the percentage of peanut allergy in high-risk pediatric groups.¹

■ Oral immunotherapy

Anagnostou and colleagues performed a randomized, controlled crossover trial evaluating the efficacy of peanut oral immunotherapy (OIT). This study focused on desensitizing children who had an existing peanut allergy. OIT can successfully induce desensitization by producing a peanut tolerability in most children with a known peanut allergy. Anagnostou and colleagues took a sample of 104 children between ages 7 and 16 years who had either a significant reaction to peanuts upon ingestion, positive allergy skin tests to peanuts, or positive allergy skin testing that was done by a “double-blind placebo-controlled” trial.⁹

When the children were desensitized, there were also immunologic changes. Thirty-nine children with a known peanut allergy sustained routine ingestion of 800 mg peanut protein on a routine basis. Of the 39 children, 24 of them were desensitized to peanuts at the conclusion of the trial. Peanut OIT raises the

reactive threshold at least 25 times so that over 90% of children can tolerate daily ingestion of 800 mg protein; more than 60% of children can tolerate 1,400 mg of protein, which equates to approximately 10 peanuts.⁹

■ Peanut sublingual immunotherapy results

A randomized control trial examined the immunologic effects of peanut sublingual immunotherapy (SLIT). According to Kim and colleagues, SLIT therapy is safe and efficient in the desensitization of peanut allergies in children.¹⁰ The trial found that 47 children ages 1 to 11 years who had a previous diagnosis of peanut allergy (including a positive immunoglobulin E [IgE]) participated in ingesting 5,000 mg of protein from peanuts to assess the efficacy of desensitizing children.¹⁰ The 25 participants who completed the trial had sustained unresponsiveness after 5 years of treatment. It was concluded that intervening early with the SLIT method could raise permanent desensitization to food allergies.¹⁰

■ Early OIT in peanut-allergic preschool children

In a subsequent study, Vickery and colleagues found that OIT was a safe and effective means of suppressing the allergic immunologic response to peanuts in young children.¹¹ The study consisted of preschool and younger age children with a known peanut allergy.¹¹ Forty children with known or suspected peanut allergy were enrolled in the study and ranged in age from 9 months to 36 months.¹¹ Children who did not react to peanuts during a food challenge were excluded.

Children qualifying for the study were randomized 1:1 and received early OIT in a double-blind manner.¹¹ Peanut-specific IgE levels significantly declined in the children treated with early OIT and were 19 times more likely to successfully consume dietary peanut than the matched standard-care controls.¹¹ Researchers found that allergic adverse reactions were common with early OIT but generally mild in nature.¹¹

■ Safety of a peanut OIT protocol

Hofmann and colleagues studied 28 children and adolescent ages 1 to 16 years to evaluate the safety of patients enrolled in a peanut OIT study. Twenty of the initial patients completed the duration of the study.¹² Reactions from several body systems were recorded both in the clinical setting upon introduction and escalation as well as at home during the “home phase” of the study.¹²

On the escalation day, upper respiratory tract (79%) and abdominal (68%) symptoms were the most commonly recorded.¹² The risk of mild wheezing during the escalation day was 18%. The risk of reaction during the home phase was 3.5% and consisted of upper respiratory tract (1.2%) and skin (1.1%) symptoms being most common. Treatment was given with 0.7% of home doses, and the most common treatments were diphenhydramine followed by albuterol. Two subjects received epinephrine after one home dose each.¹²

■ Peanut OIT for moderate-to-severe allergy

Kukkonen and colleagues enrolled 60 patients ages 6 to 18 years who had a moderate-to-severe reaction to a double-blind placebo-controlled peanut challenge. The researchers placed 39 subjects into the OIT group. Those subjects received the oral therapy during an 8-month buildup and maintenance phase. The control group was comprised of 21 patients who avoided peanuts.¹³ This study measured specific IgE and immunoglobulin G4 (IgG4) to peanuts and also monitored adverse reactions. The median follow-up period for the trial was 30 months.¹³

Eighty-five percent of the OIT patients passed the buildup phase, and 67% tolerated 5 g of peanuts during the posttreatment challenge. During OIT, IgE-to-peanut decreased and IgG4 increased. The annual incidence rate of ED visits during the follow-up period was 11% (3.0 per 10,000 patient days).¹³ Peanut OIT was found to be efficacious in severe peanut allergies without the adverse reactions on airway inflammation levels.¹³

■ Epicutaneous immunotherapy

A recent trial conducted by Jones and colleagues concluded that epicutaneous immunotherapy (EPIT) for peanut allergy was both safe and effective.¹⁴ After a 52-week study of 74 patients ages 4 to 25 years, the researchers noted that those in the EPIT group had reduced basophil activation, reduced peanut-specific T helper cell type 2 cytokines, and increases in peanut-specific IgG4 levels and IgG4/IgE ratios.¹⁴ They further noted that while there was a 79% reaction rate in patients receiving the immunotherapy, the reactions were predominantly local-patch site and mild reactions.¹⁴

The researchers concluded that there is a modest treatment response, with the highest responses among younger children. There was a strong adherence and retention rate with EPIT as well as significant changes

in immune pathways that would signal positive changes for those allergic to peanut proteins.¹⁴

■ Discussion

Many new approaches are being trialed with the primary focus of food allergies, such as peanuts and other IgE-mediated foods. OIT has shown in clinical trials to be a superior and efficient treatment in the reduction of many of the IgE-mediated food allergies, such as milk, egg, and peanuts. With desensitization for known peanut allergies, clinicians may be able to reduce the incidence of anaphylaxis and other severe reactions in the future for children by making the reactions less severe. It would also prevent the possibility of developing tolerance when treatment is discontinued. Although OIT has not been shown to be 100% effective, it offers the potential for an increased quality of life for severe food-allergy sufferers.

Du Toit and colleagues concluded that when peanuts are introduced earlier in childhood, there may be a reduction in the prevalence of peanut allergies in children who are at a high risk of having peanut allergies (as long as it was in a controlled setting).¹ Vickery and colleagues concluded from multiple studies that peanut OIT is both safe and effective.¹¹ Their research indicated that the participants in one trial successfully sustained peanut desensitization 5 years after sublingual OIT. A subsequent study showed that preschool-age children were 19 times more likely to consume peanuts with no adverse reactions than those in the placebo group.¹¹

With regards to safety, Hofmann and colleagues found a meager percentage of severe reactions outside the initial or escalation phase of OIT, and less than 1% of patients required any treatment for reactions during the home use phase of the study.¹² Kukkonen and colleagues studied airway inflammation specifically and found that OIT was efficacious in severe peanut allergies without negative effects on airway inflammation.¹³

A trial of 74 patients performed by Jones and colleagues found that while there was a 79% reaction rate to the administration of the EPIT during the trial, those reactions were very mild. Patients typically had minimal reactions, which were noted to include local-patch site reactions and other minor skin issues. No respiratory events were reported.¹⁴

More research is needed to determine the outcomes when therapy is discontinued or when other children, who do not meet the criteria for the standards of Du

Toits trial, participate in the desensitization process.¹ Safety needs to be addressed further regarding the types of reactions and what is required to treat the known reactions. This will allow protocols to be initiated for training providers who may choose to introduce this novel and still experimental treatment, which has yet to be approved by the FDA.

■ Implications for practice

Children who are at high risk for peanut allergies should be reevaluated and frequently assessed for a recurrent allergic reaction when being desensitized as part of the management. When the child is in the desensitizing level, there should be individualized controls that ensure the treatment therapy is appropriate. The clinician must also pay particular attention to comorbidities such as asthma, allergic dermatitis, and allergic rhinitis. Ongoing education regarding peanut allergies is needed to reiterate the importance of emergency treatment and recognition of life-threatening allergic reactions as well as the proper administration of the epinephrine autoinjector.¹⁵

New epinephrine autoinjectors, such as Auvi-Q, have come onto the market and are more cost effective and provide an audio recording to help patients administer the product properly.¹⁶ Practice considerations also include safely monitoring and administering OIT.⁹ OIT needs to be performed in a clinical setting with safe guidelines, proper monitoring, and personnel who are adequately trained and knowledgeable in managing allergic reactions and medical emergencies, including advanced airway emergencies due to the potential risk for anaphylaxis. OIT has been shown to be a suitable therapy for patients treated by an allergy and asthma specialized professional specifically related to food allergies.¹⁷ OIT is still considered investigational for the treatment of peanut allergies due to the potential adverse events.¹⁸

Larger, randomized, placebo-controlled trials need to be completed and should be performed with the primary focus on high-risk pediatric populations to determine the efficaciousness and both the short- and long-term safety of OIT before it can be safely implemented in clinical practice settings. After a better understanding of administration, reactions, and tolerance, it could be possible to expand the role to clinicians in primary practice settings. This would further advance the availability of lifesaving therapies to the most vulnerable individuals in our population. ■

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