Interventional Therapies for the Treatment of Food Allergy

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KEYWORDS

• Food allergy treatment • IgE-mediated food allergy • Oral immunotherapy • OIT • Sublingual immunotherapy • SLIT • Epicutaneous immunotherapy • EPIT

KEY POINTS

- Approved treatment of IgE-mediated food allergy is currently limited to allergen avoidance and emergency treatment with epinephrine on accidental ingestion.
- Oral immunotherapy has shown promise in recent studies. Most patients achieve successful desensitization but adverse effects are common, including gastrointestinal symptoms and anaphylaxis.
- Sublingual immunotherapy and epicutaneous immunotherapy seem to offer improved safety profiles but lower efficacy.

Food allergy is an increasingly common problem, with an estimated prevalence of up to 8% among young children and 3% to 6% of the entire US population.[1–3] In recent decades, prevalence has increased, especially for peanut allergy.[3,4] The natural history of food allergy leads to natural tolerance for some children, but allergies to peanuts and tree nuts usually persist into adulthood.[5] Milk and egg allergy may also persist, especially among those most severely affected.[6,7] Although life-threatening anaphylactic reactions to foods do occur, overall mortality due to food allergy is rare.[8] Evidence is ample, however, that food allergy has a significant impact on

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affected individuals and family members, through morbidity and negative effects on quality of life.[9,10] Approved management of food allergy is limited to allergen avoidance and administration of rescue medications, such as antihistamines and self-injectable epinephrine as needed when reactions occur. Together, all these factors illustrate the need for an effective therapy for food allergy.

Although reports of successful oral immunotherapy (OIT) for food allergy date to at least 1908,[11] this approach was never widely adopted. In the 1990s, attempts to desensitize or promote tolerance through subcutaneous immunotherapy did show increased tolerance to oral peanut challenge, but rates of severe reactions were unacceptably high.[12,13] Interest in interventional therapies for food allergies has increased recently, with substantial research efforts undertaken to investigate multiple forms of immunotherapy (oral, sublingual, and epicutaneous). Although the Food and Drug Administration (FDA) has not yet approved any interventional therapy for food allergy, this article reviews the progress to date and discusses future prospects in the search for safe, reliable treatment options for food allergy.

IMMUNOTHERAPY

Oral Immunotherapy

OIT has received more attention and currently has a larger evidence base than sublingual immunotherapy (SLIT) or epicutaneous immunotherapy (EPIT). Protocols vary, but the general approach typically involves 3 phases:

- Initial escalation
- Buildup
- Maintenance

Initial escalation dosing is generally performed in a single day with 6 to 8 increasing doses. Doses usually start at less than 1 mg and increase to several milligrams. In the buildup phase, patients ingest a daily dose of the food allergen, which is increased at regular intervals until reaching the target dose. This dose (typically several hundred milligrams or more) is then continued for the duration of the maintenance phase. An oral food challenge (OFC) at the end of maintenance assesses for desensitization, a temporary state of immune unresponsiveness with an increased threshold of reactivity. For those who are successfully desensitized, an additional OFC may be done after a period of abstinence to assess for sustained unresponsiveness (SU). Many patients are desensitized during OIT, but fewer seem to achieve SU, although this has not been significantly addressed in most published studies.

Peanut oral immunotherapy

Interest in peanut OIT has increased significantly, beginning with case reports of successful peanut OIT published in 2006.[14,15] The first multicenter randomized peanut double-blind placebo-controlled (DBPC) peanut OIT study was reported in 2011.[16] Sixteen of 19 children (age 1–16) in the active treatment arm achieved desensitization, passing a 5000-mg peanut DBPC food challenge (DBPCFC) after 48 weeks OIT with a maintenance dose of 4000-mg peanut protein. The other 3 subjects withdrew due to allergic side effects.

SU after peanut OIT was first reported by Vickery and colleagues[17] in 2014. In this open-label peanut OIT trial, children (age 1–16) were treated for up to 5 years with a peanut OIT maintenance dose of up to 4 g peanut protein per day. Twelve of 24 patients who completed the protocol achieved SU (passed 5 g OFC) 1 month after stopping OIT. Those who passed had lower levels at baseline and at time of challenge of