

Evaluation of the Efficacy and Safety of Oral Immunotherapy with Peanut (*Arachis hypogaea*) in Children with Food Allergy

Summary

The prevalence of food allergies among children in highly developed countries has been steadily increasing. Peanuts, the seeds of the peanut plant (*Arachis hypogaea*), are among the most common food allergens and a leading cause of severe, life-threatening anaphylactic reactions. Current recommendations for patients with peanut allergy include strict allergen avoidance and access to emergency medication for anaphylaxis, above all an adrenaline auto-injector. Over recent decades, numerous studies have investigated the development of allergen-specific immunotherapy for patients with peanut allergy. Food immunotherapy is a causal treatment for food allergy, aimed at raising the reaction threshold to the allergen and reducing the risk of severe allergic reactions following accidental exposure. Allergy societies, including the European Academy of Allergy and Clinical Immunology (EAACI), recommend oral immunotherapy as a treatment for children and adolescents with IgE-mediated peanut allergy. Despite the growing body of evidence on the efficacy and safety of this approach, the therapy had not previously been administered or clinically evaluated in Poland. The present work reports the first use of oral immunotherapy for peanut allergy in children in Poland, together with an assessment of its efficacy and safety.

Allergen immunotherapy for food allergy involves the regular administration of increasing doses of the offending food in order to induce immune tolerance. It may be delivered via the oral (OIT), sublingual, epicutaneous, or subcutaneous route. The oral route is the most extensively studied form of food allergen immunotherapy. Peanuts are used in various forms, including flour, powder, peanut butter, and whole peanuts. The introduction into clinical practice (mainly in the United States) of Palforzia, a preparation containing peanut protein intended for oral therapy, marked an important milestone in the development of allergen-specific immunotherapy for peanut allergy. Results of clinical trials to date indicate that OIT is effective and has an acceptable safety profile in patients with peanut allergy. At the same time, data on the efficacy and safety of OIT for this indication in the paediatric population of Central and Eastern Europe, including Poland, remain limited.

Another significant challenge in the use of OIT is the lack of standardised procedures, both for patient selection and for the desensitisation process itself. Published studies have used a variety of treatment protocols, differing in starting and maintenance doses, rate of dose escalation, and the duration of individual treatment phases. Such variability limits the direct comparability of study outcomes and complicates the identification of the optimal OIT strategy for everyday clinical practice. To address these limitations and the identified gap in the available data, a study was designed to evaluate the efficacy and safety of OIT for peanut allergy in the Polish paediatric population and to compare two maintenance doses: 150 mg and 300 mg of peanut protein. The study also aimed to determine whether a higher maintenance dose provides a greater level of protection against allergic reactions in the event of accidental exposure. The findings may contribute to a better understanding of the potential of OIT in children and provide data to help identify the optimal maintenance dose in this patient group.

This doctoral dissertation comprises a series of three thematically related publications which together reflect the successive stages of the research – from a review of the current state of knowledge, through an analysis of patient eligibility criteria, to an evaluation of the outcomes of immunotherapy.

The first publication reviews the current state of knowledge on peanut protein immunotherapy. It discusses the main routes of allergen administration used in desensitisation: oral, sublingual, and epicutaneous. For each method, data on efficacy and safety are presented, along with the potential risks and benefits associated with its use.

The second paper analyses the eligibility criteria for allergen-specific immunotherapy. In most published studies, enrolment in desensitisation is preceded by an oral food challenge (OFC) to confirm the allergy. This procedure carries a risk of adverse events, including severe, life-threatening anaphylaxis. In search of a safer alternative to food challenges, data from 74 OFCs performed to assess eligibility for immunotherapy were analysed. Cut-off values were proposed for individual immunological markers (skin prick tests, SPT, and specific immunoglobulin E, sIgE), which, combined with clinical history, may allow more precise selection of patients for treatment and, in some cases, eliminate the need for an oral food challenge. Particular attention was paid to component-resolved diagnostics, assessing the utility of sIgE levels to individual allergen components for qualifying patients for immunotherapy.

The next publication, which summarises the outcomes of the treatment process, evaluates the efficacy and safety of allergen-specific immunotherapy using two maintenance doses: 150 mg

and 300 mg of peanut protein. A total of 44 paediatric patients over 4 years of age underwent immunotherapy. The primary endpoint, defined as tolerance of ≥ 300 mg of peanut protein in a single dose, was achieved by 73.9% of patients receiving the 150 mg maintenance dose and 71.4% of those receiving 300 mg. Both dosing regimens were associated with favourable changes in markers of immune tolerance, including reduced SPT reactivity, decreased sIgE levels to peanut components, and increased levels of specific immunoglobulin G4 (IgG4). These findings indicate immunological changes characteristic of the acquisition of allergen tolerance.

The therapy showed a favourable safety profile, and the adverse events observed were mostly mild or moderate.

The results confirm that oral immunotherapy effectively raises the threshold of tolerance to the allergen and induces favourable changes in immunological parameters. The comparison of the two maintenance doses showed no significant difference in the proportion of patients reaching the primary endpoint. This suggests that both doses may be effective in achieving desensitisation while maintaining an acceptable safety profile. Component-resolved diagnostics is a valuable, though not yet sufficient, complement to the oral food challenge.

Taken together, the data support the gradual introduction of oral immunotherapy for peanut allergy into clinical practice, particularly in specialised centres experienced in the diagnosis and treatment of food allergy.