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Oral immunotherapy for peanut allergy: an evidence-based medicine assessment

See linked article by Sheikh *et al*. on pg 41

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Food-induced allergic disorders mediated by IgE represent a major health problem, affecting children and adults worldwide.[1] Even though the exact prevalence of food allergy is difficult to determine, it has been reported that in some countries IgE-mediated food allergy affects up to 6-8% of children and up to 2-4% of adults.[1-3] Some food allergies such as egg, milk, soy and wheat may be outgrown within the first decade of life, whilst others such as peanut, tree nuts, fish and shellfish are often lifelong.[4] Food allergy has different clinical manifestations involving many body systems including the skin, the gastrointestinal and respiratory tracts, and the cardiovascular system. Furthermore, the incidence of food-related anaphylaxis primarily in children seems to be increasing globally. Individuals with both severe or difficult asthma and a history of food allergy are those at highest risk of developing life-threatening anaphylactic reactions.

One of the major food allergens in many countries is peanut.[5,6] Peanuts are widely used as a nutritious oral aliment (providing protein, vitamins and minerals) and are the most common food-related cause of IgE-mediated allergic reactions.[7] Patients with atopic dermatitis can increase their risk to sensitisation to peanuts and subsequently the development of peanut allergy due to cutaneous exposure to peanut oil-containing creams.[8] Reactions to peanuts are immediate and can be severe, even life-threatening. Symptoms range from a relatively mild urticarial rash, vomiting, diarrhoea, wheezing, and dyspnoea, to severe throat angioedema, cardiovascular collapse or fulminant anaphylaxis.[9] Patients with well-documented peanut allergy often have to carry rescue medication such as adrenaline auto-injectors to treat themselves if severe reactions occur.[9] Measures to prevent (or even cure) food allergies such as peanut allergy are therefore a high scientific priority in the field of allergic disease, and many attempts to induce tolerance to peanut are under way.

In this issue of the *Primary Care Respiratory Journal,* Sheikh and colleagues present a timely systematic review[10] of studies that have attempted to induce desensitisation and tolerance to peanut by oral immunotherapy in patients with such allergy. A thorough search of the major biomedical databases was conducted using a previously designed study protocol. In total, 1,672 potentially eligible studies were identified. After a systematic evaluation, only six studies met the study inclusion criteria, enrolling 85 patients in total. Surprisingly, the duration of oral immunotherapy treatment varied between studies, ranging from 6 days to 36 months. Four studies were multicentre and two single centre. Four studies were conducted in the USA and two in Europe. All studies used a "case series" design, and so this systematic review lacks the strength that can be provided by randomised prospective placebo-controlled studies. This situation was stated by the authors to be at high risk of bias. Regardless, the studies overall argue that oral immunotherapy may have some future, since the treated patients tolerated higher doses of peanut after the

immunotherapy treatment. This could be a promising new therapeutic intervention for the short- to medium-term management of well selected patients. It is stated that this treatment should always be given in clinical settings and patients should be monitored carefully.

The authors wisely conclude[10] that the science suggests that this approach has indeed potential, but many obstacles remain. So far, immunotherapy for food allergens, including peanut, is an experimental therapy in specialist centres. Robust evidence-based medicine data is required.

It is important to consider that in order to achieve successful results in terms of tolerance and desensitisation after using allergen specific immunotherapy, the dose of allergen given to the patient should be at high doses. This implies an innate risk of inducing severe systemic adverse reactions including anaphylaxis. Therefore, in some specific cases such as asthmatic patients with peanut allergy, it may be worth evaluating the use of anti-IgE therapy as combination treatment with allergen immunotherapy. This may allow higher doses of immunotherapy to be achieved more rapidly in a safe manner.

Oral immunotherapy for food allergy is a new approach in the treatment of allergic diseases. This systematic review[10] shows the urgent need in the field of food allergy to conduct well-designed and well-powered studies using proper standardised allergens. Serious attention should be focused on various methodological issues including:

(i) the selection of patients
(ii) the design of the studies
(iii) the selection of validated outcomes for the evaluation of effectiveness
(iv) the statistical analyses
(v) the duration of treatment, and
(vi) the evaluation of safety.

Due to the nature of food allergies, future cost-effective studies are mandatory.

Conflicts of interest The authors declare that there are no conflicts of interest in relation to this article.

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Single inhaler maintenance and reliever therapy (SMART) in general practice asthma management: where are we?

See linked article by Riemersma *et al*. on pg 50

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Despite effective pharmacological options for treating asthma, most patients fail to achieve good control.[1] Non-adherence is common, with over-reliance on short-acting β_2-agonists (SABA) and under-use of inhaled corticosteroids (ICS) frequently being observed.[2] There is a real need to consider new approaches to improve outcomes.

One approach that has attracted attention and controversy is Single inhaler Maintenance And Reliever Therapy (SMART) using the budesonide-formoterol combination inhaler Symbicort™. SMART is advocated by proponents on both pragmatic and theoretical grounds,[3] and its use in primary care is addressed by Riemersma *et al*. in this issue of the *PCRJ*.[4]

In the traditional 'step-wise' asthma guideline model, therapy classes are added and doses increased when control is not achieved. Most patients use regular ICS 'preventer' treatment and an additional SABA inhaler used on an 'as-needed' basis; but when patients remain uncontrolled on ICS, long-acting β_2-agonist (LABA) treatment is added, increasingly in the form of a fixed-dose ICS/LABA combination