Oral Immunotherapy for Food Allergy in Children

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Classically, avoidance of food allergens has been the mainstay of management for children with severe food allergies. The application of immunotherapy for food allergies provides hope for children with severe allergies to help desensitise them, reducing the risk of a reaction and improve quality of life for both patients and carers.[1]

Immediate or IgE-mediated food allergies are common across Europe and affect 4–8% of children and 3–4% of adults.[2] They are the leading cause of anaphylaxis of children in Europe.[3] It is therefore unsurprising that food allergies present both a burden to healthcare systems, as well as having substantial psychological impact and reducing quality of life for parents and carers alike.[4]

For most children with IgE-mediated allergies to food, management has conventionally involved allergen avoidance and carrying an EpiPen should accidental contact occur. However, the development of immunotherapy has provided a positive avenue of management for some children with food allergies. Immunotherapy involves gradual exposure to small amounts of an allergen, which over time is increased in order to prompt desensitisation. The 3 main types of immunotherapy associated with food allergen desensitisation are: oral immunotherapy (OIT), sublingual immunotherapy (SLIT) and epicutaneous immunotherapy (EPIT).[1] This article will focus on OIT.

Background

OIT involves exposing a child to a food allergen through ingestion; a child will be given a small amount of allergen to eat or drink. The allergen may be in liquid or powder form and often mixed with drink or food, such as yoghurt. The continued exposure to the allergen involves dose escalation, whereby the volume given is slowly increased daily or every few days, providing no reaction occurs. The aim is to reach a 'maintenance dose', whereby a child can tolerate a maximum dose without reaction. The maintenance dose needs to be maintained daily for a considerable amount of time – on some occasions more than a year – in order to maintain tolerance. For some children, after this time, they can reduce exposures to around 3 times per week without affecting tolerance. However, continued exposure remains a lifelong practice to avoid the chance of increasing risk of reaction.[1]

Effectiveness of OIT is shown to be affected by a child's age; it is more successful in younger children. Currently, the main body of evidence supports the effectiveness of food-related OIT for peanut, cows' milk and egg. However, in theory, it is expected that OIT can be applied to a multitude of food proteins as well as for medication allergies, such as for allergies to antibiotics.[1]

OIT for peanut allergy

It is thought that approximately 1–2% of children in the UK are affected by a peanut allergy.[5] Frequently triggering life threatening reactions, it is an allergy which is often severe and can last a lifetime.[6] As well as physical reactions, the stress associated with managing a severe peanut allergy can significantly reduce quality of life for both patients and caregivers.[7]

There is evidence that the use of OIT can help to reduce the severity of peanut allergies in children. When looking into the effectiveness of OIT for peanut allergy, a 2022 guideline found that children undergoing OIT were six times more likely to tolerate a single dose of 300 mg and 17 times more likely to tolerate 1000 mg of peanut after treatment in comparison to an initially tolerated 34 mg prior to enrolment. As a result, the Global Allergy and Asthma European Network (GA2LEN) went on to recommend that OIT for peanut allergy be offered under specialist supervision, with evidence-based protocols and licenced pharmaceutical products.[8]

Another study from the same year found that OIT using peanut flour led to 21% of children who had actively received treatment eating peanuts six months after treatment without having an allergic reaction and were considered to be in remission. This was in comparison to a remission rate of 2% for children receiving placebo flour. The study also found that the youngest children, and those who started the trial with lower levels of peanut-specific antibodies, were most likely to achieve remission.[9]

Currently, the only OIT available on the NHS for peanut allergy is Palforzia.[1] In 2022, the National Institute for Health and Care Excellence (NICE) recommended the use of Palforzia for desensitising children and young people between the ages of 4 and 17 with peanut allergy.[10] Palforzia comes in capsule form,[1] contains defatted peanut powder, and comes in escalating doses of peanut which is released over time until a maintenance dose of 300 mg/day (1.5 peanuts) is reached.[10] Palforzia has a ~60–70% successful desensitisation rate for children and young people who react to approximately half a peanuts worth, ≤100 mg peanut protein.[11] The treatment is thought to reduce the anxiety around accidentally eating peanut owing to the fact that reduced risk of severe reaction occurs if exposed.[12]

Whilst, no doubt, the advancement of application for OIT for the management of peanut allergy has provided a positive avenue for many patients and carers, thoughts on long-term management and on-going monitoring and support of peanut allergy following initial OIT may have sadly been ignored. OIT requires intensive healthcare investment; the treatment pathway involves multiple visits for dose escalation, up-dosing, monitoring of patients taking maintenance therapy and conversion onto daily real-world peanut consumption. The current demand for peanut immunotherapy exceeds availability for the service.[14]

As a result, The Delphi exercise was designed to achieve a consensus guidance to inform and support healthcare professionals (HCPs) in the safe implementation of Palforzia desensitisation and ongoing peanut dosing after OIT completion.[13] This consensus highlighted the crucial need for the NHS to increase capacity for undertaking diagnostic food challenges, as well as developing Palforzia immunotherapy pathways with consideration for more flexible care pathways to support adolescents in particular. It was highlighted that trusts must offer a multidisciplinary approach and ensure follow-up for patients after establishing maintenance therapy. Evidence shows there is a need to ensure adequate health service infrastructure, training for staff and dissemination of best practice to optimise outcomes for patients with peanut allergy in the NHS.[13]

Cows' milk & egg allergies

Cows' milk and egg allergies present very commonly in young children. In comparison to peanut allergy which can be lifelong, most children outgrow milk and egg allergies by the age of 5, although, in some cases, the allergies can persist.[1] The use of a 'ladder' to reintroduce milk/egg has routinely been used as a way of desensitisation for mild to moderate milk and egg allergies for many years. The ladders begin with milk or egg in a highly cooked form, building up volumes and introducing increasingly less cooked milk or egg.[1] After careful consideration, children can usually follow the ladders safely at home with specialist support.[1,15] For children whose milk or egg allergies are persistent or severe, OIT needs to be carried out under specialist supervision within a clinic or hospital setting.[1]

Risks of OIT

Despite OIT being a significant breakthrough in the management of severe allergies, it can still have its disadvantages. The main concern is that a child may have a significant allergic reaction;[1] at least one fatality to OIT has been reported.[16] For this reason OIT is carried out in specialist allergy clinics, so that immediate medical attention can be provided if necessary. Mild side effects may also occur, such as feeling sick and an itchy or tingling sensation in the mouth.[1]

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There are also several factors which may increase the risk of an allergic reaction whilst carrying out OIT, this includes anything which may raise heart rate as this affects how the immune system reacts to an allergen, increasing the likelihood of a reaction. It is therefore recommended that before and after treatment, exercise is avoided.[1]

It is important to be mindful that one downside of OIT is that not all children will be eligible; contraindications include if a child has uncontrolled asthma, eosinophilic esophagitis or active neoplasia, and each patient must be thoroughly assessed for suitability.[17]

It is also important to acknowledge that OIT involves considerable constraints, requires strong compliance and commitment for an extended period of time, and this in itself means it is not suitable for every child.[18]

The future

The NATASHA trial is a randomised control trial,[19] funded by the Natasha Allergy Research Foundation, and is being undertaken at nine NHS sites across the country. The clinical trial is looking at the application of oral immunotherapy for children from aged 2 with peanut or cows' milk allergies and is led by researchers at Imperial College London, Imperial College Healthcare NHS Trust, University of Southampton and University Hospital Southampton. If successful, the three-year study, which began in 2023, will provide evidence for oral immunotherapy to be made more widely available on the NHS. The trial is also training a network of NHS staff to offer this pioneering OIT to people with food allergies.[20]

Studies are now also providing evidence that immunotherapy interventions in children under 4 years of age may lead to improved outcomes and longer-term tolerance. Early oral allergen exposure has been repeatedly shown to effectively disrupt allergy maturation and prevent the development of persistent food allergy, indicating the existence of a window of opportunity. It is hoped that these studies will go on to provide evidence for optimum age for commencing OIT.[21]

Conclusion

OIT has provided both hope and a way of improving quality of life for many eligible children living with a severe food allergy, particularly peanut allergy. In order for OIT to continue to provide a beneficial avenue of management, on-going professional support and clinical infrastructure is needed in order to maintain optimum lifelong outcomes for patients. It is hoped that with further supporting evidence, OIT can be successfully applied to a whole range of food proteins and that more eligible patients can under-go treatment providing continued investment into NHS services is made.

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