

Randomised controlled trial

Oral egg immunotherapy is effective for desensitisation but not for inducing sustained tolerance in the majority of egg allergic children

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Context

Egg allergy is now one of the most common food allergies in infants and children in Australia, North America, the UK and Europe. Although the natural history of egg allergy is for tolerance and resolution in a significant portion of children, emerging trends suggest that this resolution may be less common and occur at an older age than previously believed.

Egg and egg proteins are ubiquitous and strict avoidance is both difficult and burdensome for the individual, family and school. Avoidance of allergen forms the mainstay of current treatment for food allergy. It is therefore a therapeutic priority to establish safe and effective means of desensitising or accelerating natural tolerance to food allergens. Egg allergy is an obvious target area for investigating desensitisation in food allergic individuals, owing to its prevalence and relatively lower risk of anaphylaxis per patient compared with peanut or milk allergy. Several previous smaller egg oral immunotherapy trials have reported some success in desensitising egg allergic children with daily oral egg immunotherapy. These studies have had small participant numbers, have not included a randomised placebo arm, and have had relatively short follow-up periods.

Methods

The current study is a well conducted randomised controlled study of a small number of children (n=55) which examined the efficacy of intensive oral egg immunotherapy in egg allergic children aged 5–11 years. The study encompassed 22 months of therapy and 12 months further follow-up. The primary outcome measure was sustained unresponsiveness to egg (egg white powder and whole egg), established by observed food challenge at 24 months. Secondary outcomes included clinical tolerance (desensitisation) to egg white powder at 10 and 22 months food challenge and immunological markers. Analysis was by intention to treat.

Inclusion into the study was well defined; however, children did not undergo an egg challenge as part of the entry criteria to ensure all had current clinical allergy. Treatment allocation was random in a ratio of 8:3 (40 active egg, 15 placebo). Treatment consisted of an intensive initial day escalation phase, a build-up phase, with further escalation of the previously tolerated dose and a maintenance phase, where up to one-third of an egg

equivalent in egg white powder or placebo was taken orally on a daily basis.

At 10 months, following the first oral challenge, the study was unblinded. Placebo treatment was not continued past this first time point, and children receiving placebo did not undergo further egg challenges, unless a significant reduction in their serum-specific immunoglobulin E (IgE) was detected (n=1). The children receiving egg immunotherapy were continued on their maintenance dosage irrespective of challenge outcome and underwent a further oral challenge at 22 months. Treatment was suspended for 2 months, and a further oral challenge to assess sustained tolerance of immunotherapy (oral egg) was undertaken at 24 months.

Findings

Of those children receiving active egg immunotherapy, 30 of the 40 were considered to be desensitised at 22 months and 11 of 40 were considered to have sustained unresponsiveness to egg at 24 months. None of the 15 children on placebo were considered to be desensitised at 10 months and no child on placebo was deemed to be desensitised or to have sustained unresponsiveness over the study. Seven (12%) of the study participants withdrew, five from the treatment group and two from the control group. Of the five participants who withdrew from the treatment group, four had allergic reactions to active therapy, although no severe allergic reactions were recorded.

Children who achieved sustained unresponsiveness to egg were more likely to have a decrease in skin prick test wheal size to egg over the study period. Serum-specific IgG4 levels correlated with desensitisation and sustained unresponsiveness.

Commentary

The results of this study are promising, with up to 75% of children considered desensitised during daily egg oral immunotherapy. However, the effect was only persistent for 28% of these children. Thus, for most children in this study, the oral immunotherapy would need to be continued daily for persistent protective desensitisation. Given the design of the study, with unblinding at 10 months and no exit egg challenge for all but one of the children receiving placebo, it is not possible to completely discount the effect of natural acquisition of tolerance on the study findings.

The resources involved in this intensive desensitisation protocol are substantial, as can be inferred from the relatively small number of participants in the study. Therefore, its applicability to standard clinical practice for egg allergy is currently somewhat limited by the amount of resources required to deliver safe oral food immunotherapy. This is particularly so for escalation and build-up phases and the provision of safe food

challenge environments. It is, however, proof of principle that daily oral immunotherapy in egg allergic children can render the majority of children desensitised, and can result in a state more akin to that of natural tolerance in approximately one-quarter of those children treated.

Competing interests None.