

Randomised controlled trial

Having your cake and EATing it too: early timing of multiple allergen introduction does not increase the risk of developing food allergy in standard risk, breastfed infants

10.1136/ebmed-2016-110488

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Food allergy is a chronic public health problem affecting as many as 8–10% of children and has no present cure or treatment.¹ Though delayed allergen introduction was formerly recommended that children with a family history of atopy, this strategy was later retracted given no evidence that this approach was of benefit.^{2–3} Recently, more data have emerged supporting a protective association between early allergen introduction and a reduced risk of developing food allergy in high-risk infants, but not in standard-risk children.⁴

Methods

To address this question, Perkin *et al*⁵ undertook the Enquiring About Tolerance (EAT) study. In this study, 1303 exclusively breastfed infants with no risk factors for allergic disease were randomised to two groups. The first group of infants was exposed first to milk (in the form of yogurt) and then to egg, wheat, peanut, sesame and fish in a random order at 3 months of life while the mothers were encouraged to continue breastfeeding. The aim was to introduce 4 g of protein per week for each allergen (2 servings of 2 g of protein for each allergen per week), which included cow's milk (2×40–60 g of yogurt), peanut (18 g peanut butter), fish (2 fish fingers), sesame (18 g tahini), egg (1 small egg), wheat (UK brand of 2 wheat-based biscuits (40 g), eg, Weetabix). The second group was randomised to breastfeeding until 6 months, according to the standard UK practice, and then began the same randomised introduction. Both groups were followed through age 3 to note the development of allergic disease.

Findings

In the intention-to-treat analysis (n=1132), there were no significant differences between the groups in the overall rates of developing any food allergy

(p=0.32) or rates of developing milk, egg, wheat, peanut, fish or sesame allergy. However, in the per-protocol (n=732) analysis, significantly fewer children developed any food allergy with introduction at 3 vs 6 months (2.4% vs 7.3%, p=0.01, NNT=20.4). In the per-protocol analysis, fewer children developed egg allergy (1.4% vs 5.5%, p=0.009, NNT=24.4) or peanut allergy (0% vs 2.5%, p=0.003, NNT=40) with introduction at 3 vs 6 months. Only 42.8% of participants in the early introduction group adhered to the full protocol (adherence by food, milk 85%, peanut 62%, fish 60%, sesame 51% and egg 43%). Adherence was influenced by perceived symptom development and the development of eczema.

Commentary

Overall, there was no difference in the rate of food allergy development with introduction of potentially allergenic solids at 3 vs 6 months. Though the per-protocol analysis noted a reduced rate of developing egg, peanut or any overall food allergy with introduction at 3 months, this must be interpreted cautiously because of high drop-out rates and protocol non-compliance, with strong suspicion these were motivated by reverse causality of parents concerned their child was developing signs of allergy. Optimistically, this study likely infers non-inferiority of a 3 vs 6-month timing of introduction, though it was not discretely powered to show such effects. This study also showed no adverse effects to the nutritional outcomes of the children fed an early and diverse diet, which supports earlier research.⁶

Implications for practice

The EAT study suggests that early allergen introduction in standard risk, exclusively breastfed infants is associated with small possible benefits without evidence of harm. This is a group often overlooked in studies of allergic development. These findings are generally supportive of other data in high-risk patients showing a risk-reducing benefit of early peanut introduction, and risk-reducing benefit for early egg introduction.⁴ For peanut, US clinical practice guidelines have incorporated these findings and do recommend early peanut introduction in the first year of life for standard risk children.⁷ However, the findings with respect to egg await incorporation into any clinical practice guideline worldwide.

Competing interests None declared.

Provenance and peer review Commissioned; internally peer reviewed.

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