

Partially hydrolysed whey and soy-based infant formulas did not prevent allergic disease in high-risk children

Study design

Design Randomised controlled trial.

Allocation Computer generated allocation by independent statistician.

Blinding Staff members were blind to the group of allocation at the time of outcome assessment. Parents were blinded to assigned formula until the child's second birthday.

Study question

Setting Maternity hospital in Australia.

Patients Six hundred and twenty infants with a history of allergy in a first degree relative (eczema, asthma, rhinitis, food allergy).

Intervention Infants were randomised to three groups to receive at weaning: a partially hydrolysed whey formula (pHWF), conventional cow's milk formula (CMF) or a soy-based formula.

Outcomes Primary outcome was any allergic manifestation (eczema or food reaction) assessed during telephone interviews. Secondary outcomes were individual incidence of allergies, and skin prick tests (SPTs) reactivity.

Follow-up period Outcomes were assessed at to 2 years of life. Additionally, the 2-year period prevalence of eczema, asthma and allergic rhinitis was assessed at 6 and 7 years.

Patient follow-up At 2 years, 191/206 infants allocated to pHWF were analysed; 191/208 infants were allocated to soy,

Table 1 Associations between formula and risk of allergic disease

	OR, (95% CI)	
	pHWF versus CMF	Soy versus CMF
Any allergic manifestation at 2 years	1.21 (0.81 to 1.80)	1.26 (0.84 to 1.88)
SPTs (any allergen) at 2 years	0.76 (0.46 to 1.25)	1.07 (0.66 to 1.44)
Eczema at 6–7 years	1.08 (0.69 to 1.68)	0.95 (0.60 to 1.48)
Asthma at 6–7 years	0.91 (0.57 to 1.45)	0.97 (0.61 to 1.54)
Rhinitis at 6–7 years	0.94 (0.56 to 1.58)	1.27 (0.77 to 2.10)

CMF, cow's milk formula; pHWF, partially hydrolysed whey formula; SPTs, skin prick tests.

and 193/206 were allocated to CMF. Both per protocol and intention to treat analyses were performed, without significant differences.

Main results

Overall, there was no statistically significant difference between treatment groups (table 1).

Conclusion

Partially hydrolysed whey and soy-based formulas did not reduce allergies in high-risk infants.

Abstracted from

Lowe AJ, Hosking CS, Bennett CM, *et al.* Effect of a partially hydrolyzed whey infant formula at weaning on risk of allergic disease in high-risk children: a randomized controlled trial. *J Allergy Clin Immunol* 2011;128:360–5.e4.

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Over the past few years, there has been a major paradigm shift in the thinking about the prevention of allergic disease in children. Until recently, people thought that allergy could be prevented by preventing exposure to food allergens. Clinical trials appeared to support this by showing reduced prevalence of eczema in babies fed hydrolysed formula, as compared with cow's milk formula. Several international guidelines recommended hydrolysed formula for allergy prevention, and this became common practice throughout the western world.

A few years ago, we questioned the validity of this approach by highlighting methodological shortcomings in the allergy prevention literature.¹ For example, the large differences in taste between cow's milk and hydrolysed formula preclude blinding of parents, which is important in studies with a subjective end point (eczema symptoms). In their clinical trial, Hill *et al* now reveal that inappropriate reporting of results of per-protocol analyses (instead of intention to treat analyses) may also have incorrectly made us believe that allergy

prevention by dietary measures is useful. Their well-designed (and well-analysed) study clearly demonstrates that hydrolysed formula is no more effective than cow's milk formula in preventing allergic disease in 'high risk' children.

Their results make perfect sense in the light of certain other new findings. Recent observational studies have shown lower prevalence of cow's milk and peanut allergy in children exposed to the relevant allergen in early infancy than in children in whom exposure was delayed.² Children without cow's milk allergy put on a milk-free diet may develop severe cow's milk allergy in the long run.³ Thus, in real life settings, 'allergy prevention' may be counterproductive by increasing the risk of food allergy. The current paradigm, therefore, is that early controlled exposure to food allergens is needed to develop and maintain tolerance to that food.

The time has come to admit the error of our ways, to stop medicalising healthy babies by providing them with hydrolysed formula, and to end the myth of allergy prevention by avoiding food allergens.

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