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STUDY DESIGN

Design: randomised controlled trial.

Allocation: concealed.*

Blinding: unblinded.*

STUDY QUESTION

Setting: children's hospital in Trieste, Italy.

Patients: 60 children 5–17 years of age (mean age 8 y, 65% boys) who had a history of severe allergic reaction after exposure to milk or dairy products, milk-specific serum IgE concentrations >85 kUA/l, and a positive reaction to a double-blind, placebo-controlled food challenge of ≤ 0.8 ml of whole milk. Exclusion criteria were unreliable management of complications by parents, limited access to emergency care, and poorly controlled asthma.

Intervention: specific oral tolerance induction (SOTI) (n = 30) or maintenance of a milk-free diet (n = 30). The SOTI protocol consisted of 10 days in hospital during which children were given rapidly increasing doses of milk, up to 20 ml whole milk/dose. At home, children continued with slowly increasing doses as tolerated. Parents were instructed about managing adverse reactions. Children received daily antihistamine treatment both in hospital and at home. Once the child could tolerate 150 ml whole milk, antihistamine treatment was tapered off, and consumption of other dairy products was encouraged.

Outcomes: achievement of maximum tolerance (≥ 150 ml of cow's milk in a single dose) or partial tolerance (5–149 ml) and adverse events.

Follow-up period: 1 year.

Patient follow-up: 100% (intention-to-treat analysis).

MAIN RESULTS

At 1 year, 23% of children in the SOTI group could tolerate an unrestricted diet, 13% could tolerate ≥ 150 ml of milk, 54% achieved partial tolerance, and 10% discontinued the protocol because of adverse events; no child in the control group achieved even partial tolerance (as determined by a repeat milk challenge at 1 y) (table). All children in the SOTI group had adverse events, including mouth pruritis, bronchospasm, and abdominal pain. Oral steroids were given to 27% of children in hospital and 57% at home, nebulised epinephrine to 60% in hospital and 20% at home, and intramuscular epinephrine to 13% in hospital and 3% at home (table). In the control group, 20% of children had mild reactions to accidental milk exposure.

CONCLUSION

Specific oral tolerance induction achieved at least partial tolerance to milk in 90% of children with severe cow's milk allergy.

*See glossary.

ABSTRACTED FROM

Longo G, Barbi E, Berti I, *et al.* Specific oral tolerance induction in children with very severe cow's milk-induced reactions. *J Allergy Clin Immunol* 2008;**121**:343–7.

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Specific oral tolerance induction (SOTI) v milk-free diet (control) for severe cow's milk allergy in children

Outcomes at 1 year	SOTI	Control	p Value	NNT (95% CI)*
Maximum tolerance†	37%	0%	<0.001	3 (2 to 5)
At least partial tolerance†	90%	0%	<0.001	2 (1 to 2)
NNH				
Received intramuscular epinephrine in hospital	13%	0%	0.11	Not significant
Received intramuscular epinephrine at home	3.3%	0%	1.0	Not significant

*Abbreviations defined in glossary. NNT and CI calculated from data in article.

†Maximum tolerance, ≥ 150 ml of cow's milk in a single dose; partial tolerance, 5–149 ml of cow's milk.

Food allergy has become the mainstay of clinical allergy practice in North America and western Europe. Patients often feel hopeless because of unpredictability of exposures, fear of adverse and even fatal events, and lack of effective treatments other than avoidance and emergency preparedness.¹ Because avoidance is far from foolproof, treatments to induce food tolerance are highly desirable.

Longo *et al* studied SOTI in a group of children with severe milk allergy, using rush desensitisation in hospital and continuing at home. They achieved complete or partial tolerance in 90% of children in the SOTI group and none in the control group. This finding is similar to that of Staden *et al* who used SOTI in

younger children with more moderate milk and egg allergies.² Both trials show the potential of this approach; however, SOTI is clearly not yet "ready for prime time." In the trial by Longo *et al*, although the adverse reaction rate in the hospital phase of SOTI was high, it was similar to that associated with oral food challenge in this population, which is frequently done in hospitals that specialise in food allergy.

For SOTI to be useful, patient selection is important; only severely affected patients >5 years of age are likely to be candidates. Coexisting asthma needs to be well controlled to decrease potential for lower respiratory compromise. For now, SOTI requires further study to clearly delineate the ideal

protocol and safety profile. Vaccination with modified antigens is another strategy under investigation.³ As the numbers of children with persistent food allergies increase, approaches to treatment beyond avoidance strategies are clearly needed.

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3. Burks W, Kulis M, Pons L. *Expert Opin Pharmacother* 2008;**9**:1145–52.