

Oral Desensitization with Cow's Milk in Cow's Milk Allergy. Pro!

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Introduction

The treatment of food allergies is logically based on strict elimination of causative allergens. While it is easy to eliminate food which is not frequently consumed, it is more difficult to manage an allergy involving regularly consumed foods, as hidden foods, especially when patients have to eat away from home for professional reasons. Type I allergies with IgE-dependent reactions to cow's milk proteins, dairy products and cheese are not uncommon among adults [1, 2]. In our statistics based on 402 patients with systemic IgE-mediated food allergies, celery roots were found to be the most frequent food allergen (42.8% of all cases), followed by milk and cheese (16.4%) [3]. According to serum IgE determinations by RAST, the predominant allergens in cow's milk-allergic adult patients are caseins with a sensitization frequency of 71%, whereas sensitization to whey proteins (α -lactalbumin, β -lactoglobulin) in the adult group is rare [2]. In prospective studies, tolerance to cow's milk is observed in 70–80% of infants with cow's milk allergy after 1–3 years under appropriate diet [4, 5]. On the contrary, only about 28% of cow's milk-allergic adults can hope for spontaneous desensitization by appropriate diet and can, thereafter, enjoy an unlimited symptom-free intake of milk products as it was observed after a follow-up period of 3–5 years [2, 6]. Oral desensitization with cow's milk offers in these cases an effective possibility to achieve tolerance.

Methods

Oral desensitization with cow's milk, diluted in water, was performed according to the method described in our previous publications [6–8]. Briefly, a skin prick test (SPT) end-point titration with a milk:water solution was done to establish the starting dose of oral desensitization (OD). The OD starts with 1 drop of the end-titration dose (usually 1:100 milk/water) given sublingually orally in the morning on an empty stomach. The dose was increased daily up to 10 ml (reached in 24 days) according to the desensitization schedule in figure 1. The OD was then continued with 1 drop of the next dilution (10-fold concentrated) and so on up to 250 ml of undiluted milk (fig. 2) After reaching the well-tolerated end dose the patients had to drink daily at least 1 dl of milk.

The performance of SPTs and intracutaneous tests with raw milk and milk extracts as well as of specific IgE antibodies determination to 'whole milk' (f2), α -lactalbumin (f76), β -lactoglobulin (f77) and casein (f78) are described in detail elsewhere [2]. The practice of OD with milk (OMD) is illustrated by two typical case histories:

Case 1 (B. Lilly)

The 29-year-old nonatopic female experienced for the first time at the age of 28 years an allergic episode and in the following about 20 similar episodes with cough, dyspnea, conjunctivitis, rhinitis, eyelid edema and generalized urticaria without gastrointestinal symptoms after ingestion of cheese and dairy products. She had no problems while eating butter.

Allergological examinations: SPT with undiluted raw milk was 1+ positive (wheal = 3 mm). The intracutaneous test (ICT) with cheese extract (Gruyère) (Lab. de Stallergènes, 1:10,000 w/v) resulted strong positive (wheal > 15 mm) as well as scratch tests (ST) with several brands of cheese from cow's, goat's and sheep's milk. The RASTs with milk and casein resulted class 4 strong positive.

Oral milk desensitization: Under a strict elimination diet of milk and dairy products the OMD was started with a drop of 1:100 milk:water dilution and the dose could be increased to 10 ml and then continued with the next dilutions of 1:10, 1:2, 9:1, 1:1 and undiluted milk until 250 ml.

Clinical course: At the beginning of OMD the patient experienced a chronic plugged nose. By reaching 1 dl undiluted milk, dyspnea and angioedema of the eyelids occurred. The OMD was continued with 1 dl milk under treatment with ketotifen (Zaditen) for 3 months, then without drug. After 1 year an open challenge test with 30 g Gruyère cheese was negative, but a relapse occurred 3 months later after eating 'cannelloni', a kind of pasta, with Parmesan cheese. Nevertheless, the patient was asked to drink a glass of milk every day. After 2 years she tolerated small quantities of cheese and after 3 years she could enjoy a cheese fondue! Figure 1 shows the clinical course and the results of the allergological parameters over the years. The tolerance of cheese was accompanied by negative results of the skin tests and RAST determinations.

Case 2 (Sp. Maria)

The 45-year-old, nonatopic housewife had with the age of 43 years for the first time after eating a cheese 'raclette' an acute urticaria, dyspnea, tachycardia. Again, with 44 years after cheese ingestion she developed an acute urticaria and an anaphylactic shock. In the following she experienced attacks of urticaria, dyspnea and tachycardia after ingestion of hidden milk products (e.g. in sauces, cheese in pasta, etc.). She was referred to our unit for allergy testing.

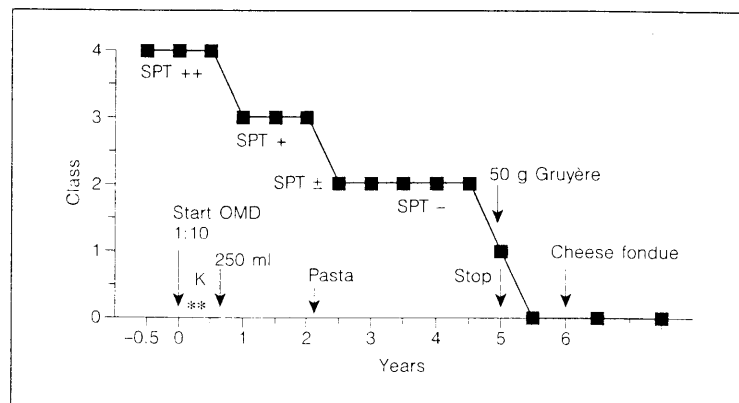
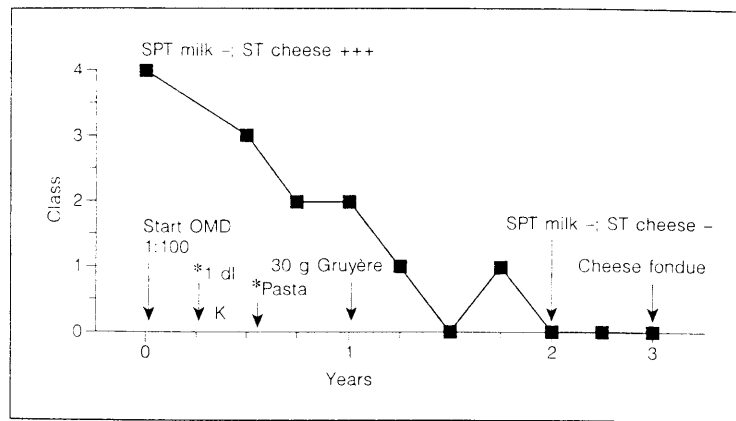


Fig. 1. Case 1 (B. Lilly, 1950): RAST class results to milk (fz Pharmacia) under ODM. *Dyspnea, eyelid edema. K = Ketotifen.

Fig. 2. Case 2 (Sp. Maria, 1934): RAST class results to milk (fz Pharmacia) under ODM. *Urticaria, cramps. K = Ketotifen.

Allergological examinations: The SPT with undiluted raw milk was 2+ positive (wheal = 6 mm). The RASTs with milk and casein resulted class 4 strong positive.

Clinical course and oral milk desensitization: After a strict elimination diet of milk and milk products the RAST test with milk still resulted class 4 positive, so an OMD was started with the concentration of 1:10 milk:water solution. By reaching the dose of 2 ml an acute urticaria occurred, so that the OMD was restarted with the concentration of 1:100. Again, by the dose of 2 ml 1:10 the urticaria reappeared. Without stopping OMD the dose could be increased in the following under ketotifen medication (1 mg bid) up to 10 ml undiluted milk.

At this point the patient tried to stop the ketotifen medication, but promptly the urticaria reappeared, so that it was decided to maintain the maintenance dose of 10 ml milk daily under ketotifen for 3 months. In this time the patient suffered periodically from stomach cramps. After 3 months the ketotifen medication was stopped and the OMD could be increased up to 250 ml milk and the patient continued the daily intake of 250 ml milk without interruption. After 2 years she tolerated Parmesan cheese on pasta. After 5 years an open oral challenge test with 50 g Gruyère cheese, performed at our unit, resulted negative. The patient could eat in the following normal cheese and enjoyed a cheese fondue! The clinical course and the results of the allergy tests performed in this prospective case study are depicted in figure 2. We can observe under OMD a continuous decrease of milk and casein-specific IgE antibodies which disappeared after 3 years. In parallel, the skin tests with milk and cheese became negative.

Results

During the years 1980–1995 the OMD was tried on 16 patients with IgE-mediated cow's milk allergy. All 16 patients were females. In 8 cases (50%), including the 2 patients described above, a complete milk tolerance was achieved after a treatment period of 3–5 years. In 4 patients (25%) only a partial tolerance was observed; the patients were able to drink without problems 10 ml of cow's milk and eat some soft cheese, but not hard cheese. The OMD had to be interrupted in 4 patients (25%), because they experienced repeated allergy reactions after intake of small quantities of the milk dilution, even under prophylactic treatment with ketotifen. As a side effect of OMD, a patient with severe asthmatic and urticaria symptoms before treatment, suffered from an erosive gastritis after drinking milk, which had to be treated with H₂ agonists (cimetidine), together with ketotifen.

Conclusions

In the allergy textbooks there is excessive criticism against oral desensitization in the treatment of food allergy [9, 10]. However, strict dietary elimination is not always possible and severe relapses can occur when eating in restaurants and canteens or in the presence of a hidden foodstuff to which a strong sensitization is present. On the other side, two-thirds of the milk-allergic patients do not recover under a strict diet and neither do the skin tests become negative, even after a follow-up period of 3–5 years [2, 6].

Cases 1 and 2 clearly demonstrate that oral desensitization with cow's milk, when successful, is not only a (subjective) tolerance, but a really immunological desensitization as demonstrated by the disappearance of IgE antibodies in skin tests and RAST. The effect is not due to an avoidance of the offending food, as patients must drink milk. So far, a placebo-controlled trial cannot be performed with oral desensitization as is the case for immunotherapy with inhalants [10].

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