

Oral rush desensitization to cow milk. Following of desensitized patients during three years

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ABSTRACT

We report the induction of tolerance in four patients with severe IgE-mediated cow's milk allergy, with an oral rush desensitization by introducing increasing daily doses of cow's milk (CM) for 5 days under clinical conditions in order to enable the patients to tolerate 200 ml of CM daily. Our results indicate that we can induce clinical tolerance in CM allergy by oral administration of progressive doses of milk. After three years of following, the four patients are taking CM with good tolerance. Specific IgE levels of casein have decreased progressively during these three years until being not detectable in three of the four patients and also a reduction has been observed in the cutaneous skin prick test reactions to CM.

Key words: Cow's milk allergy. Induction of tolerance. Oral rush desensitization.

INTRODUCTION

IgE-mediated allergy to cow's milk proteins (CMP) is common in the atopic infant and often is the first manifestation of food allergy¹. By the age of 5, most children outgrow this hypersensitivity but about 15 % retain their sensitivity in the second decade of life, being considered bad prognostic indexes the remaining of CM allergy at the age of five, high levels of CM and casein specific IgE and certain allergenic epitopes of CMP^{2,3}. Until now, the basic treatment is the complete avoidance of CMP. Because of the widespread use of them in food, this approach is often difficult. Diet failures and accidental introduction are not uncommon and they can be potentially severe. Therefore, we need to look for new therapeutic regimens. Oral desensitization with CM was introduced early in the therapy of CM allergy. Schemes for CMP desensitization were normally performed over many weeks⁴⁻⁶. In 1999 Bauer published the induction of tolerance with a 5-day oral rush desensitization (ORD) under clinical conditions⁷. Our aim was to carry out an allergological and clinical following to four CMP allergic patients who were desensitized to CMP with a modified Bauer's oral rush protocol three years ago.

CASE REPORT

We performed an oral rush desensitization in four children with IgE-mediated allergy to CMP (diagnosed with positive skin prick test (SPT), specific CM and casein IgE and a positive double-blind placebo-controlled challenge test the week before the desensitization): patient n.º 1: a 2 year-old boy, with casein specific IgE of 52.2 KU/l; patient n.º 2: a

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2 year-old girl with casein specific IgE of 3.48 KU/l; patient n.º 3: a 19 months girl with casein specific IgE of 4.82 KU/l and patient n.º 4: a 5 year-old boy with casein specific IgE of 5.11 KU/l. The clinical reaction to CMP in the first three cases was anaphylaxis with urticaria, angioedema, vomits and bronchospasm and in the fourth case urticaria and vomits. The first two cases also presented allergy to egg.

Following the protocol suggested by Bauer⁷ et al with small modifications in order to adapt to our clinical assistance, we performed oral desensitization with cow milk for 5 days under clinical conditions at hospital, previous paternal informed consent, starting the first day with 1 ml of diluted cow milk 1/100, doubling the dose every hour, with 5 doses per day: 1-2-4-8 and 16 ml 1/100; Second day every hour: 16-32 ml 1/100 and 6-12-24 ml 1/10; Third day every hour: 24-48 ml 1/10 and 8-16-32 ml of undiluted CM; Fourth day only 3 doses, every 2 hours: 32-64 and 100 ml of CM; The last day only 2 doses, every 2 hours: 100 and finally 200 ml of CM. The procedure was well tolerated by all the patients. After

some of the doses they presented erythema or urticarial elements around the mouth that were solved in few minutes and one patient presented cough and wheezing with the dose of 16 ml of CM, solved with salbutamol in a few minutes, but he could continue the protocol. At the end of the protocol they were assorted to take at least 200 ml of CM daily. One of the patients, presented abdominal pain and oropharyngeal itching the tenth day with the taking of CM for what the administration was discontinued, and then it was begun 21 days later with a slow increment of the doses each 3 to 7 days.

We carried out a clinical following of desensitized patients with SPT and specific IgE determination at 1 month, 6 months, 1, 2 and 3 years after desensitization.

At the present time, after three years of following, the four patients are taking CM with good tolerance. The levels of casein specific IgE have decreased progressively during these three years until being not detectable in three of the four patients (fig. 1) and also a reduction has been observed in the cutaneous SPT reactions to CM (table I).

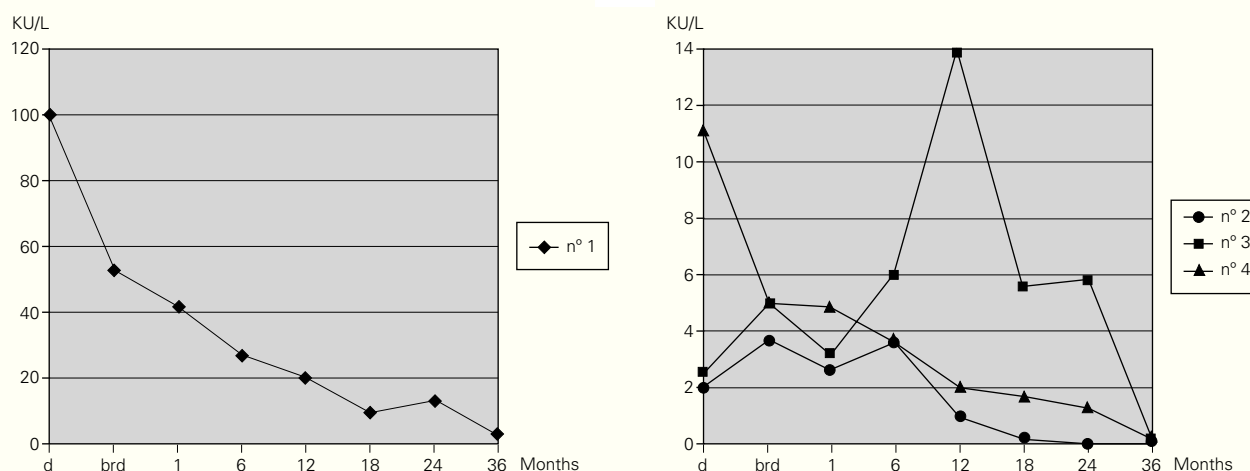


Figure 1.—Evolution of specific IgE levels of casein (KU/l) in the patients that followed the oral rush desensitization. d: diagnosis; brd: before beginning ORD. The value 100 correspond to > 100 KU/l levels.

Table I

Results of skin prick test (SPT) with cow's milk dilutions (1/1000, 1/100, 1/10 and 1/1). Represented by the maximum dilution SPT was positive

Patient	Before desensitization	1 month	6 month	18 months	24 months	36 months
1	+1/1000	+1/1	+1/1	+1/10	+1/1	+1/1
2	+1/10	+1/10	+1/10	+1/1	+1/1	—
3	+1/10	+1/1	—	+1/1	—	—
4	+1/1000	+1/10	NR	+1/1	+1/10	+1/10

NR: not realized. (—): negative.

DISCUSSION

When CM is diagnosed, a strict elimination diet is the choice therapy at the moment. It seems quite a bit simple but all we know is very difficult for many parents and patients due to the hidden food and many times not labelled in many commercial foods, so frequent diet failures and accidental introduction are not uncommon and they can be potentially severe for these patients. In order to solve these problems the possibility of reaching food tolerance with oral desensitization has been attempted with successful results. Patriarca et al reported successful results in four of six children, until reaching 120 ml of CM on day 104⁴. As in our results, they observed important and progressive reduction in SPT and casein specific IgE at 6, 12 and 18 months after oral desensitization.

In 1999 Bauer et al published the induction of tolerance on a 12-year-old girl with persistent IgE-mediated cow's milk protein allergy with a 5-day oral rush desensitization under strict clinical conditions⁷. We have adapted this protocol to our clinical practice, with successful result in all our four patients.

Meglio et al successfully desensitized 15 of 21 children in a period of six months increasing daily doses of CM. They stress the importance of the partial outcome of three of 21 children who could not reach the maximum account of 200 ml/day, but were able to tolerate 40-80 ml/day so they dramatically reduced the risk of severe reactions after accidental or unnoticed introduction of low quantities of CM. At the end of desensitization they observed a reduction in cutaneous sensitivity in the SPT to CM, but they observed no significant differences in CM, casein and betalactoglobuline specific IgE in relation to previous specific IgE⁶. It is according to our results, since the reduction of IgE levels reach a significant decrease in a longer time of following.

We have had a successful result in cent per cent of patients, and after three years of following, the four patients are taking CM with good tolerance, and we have had no reports of more allergic reaction to CM in these patients. However it has been recently reported by Caminiti et al a food-exercise induced anaphylaxis in a patient successfully desensitized to CM, who was tolerating until 300 ml of CM, but on two occasions, 30 minutes after having breakfast

with milk ingestion the boy participated in a football match and developed suddenly an anaphylaxis. After these episodes the patient continues tolerating CM as well as exercise if he avoids milk at least 3 hours before any exercise. They notice and advice that achievement of induced tolerance to milk may be only partial and that the tolerance can be overcome by a relevant non specific stimulus like exercise⁸.

We have observed a reduction in sensitization to CMP in our patients. In two patients (50 %) the SPT and specific CM and casein IgE have become negative, what may reduce the probability of previously described reactions.

Our results indicate that we can induce clinical tolerance in CM allergy by oral administration of progressive doses of milk.

It is a therapeutic possibility that allows advancing the clinical tolerance to CM, although more experience should be accumulated with the purpose of valuing their effectiveness and security in the routine of treatment of CMP allergy.

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