Sublingual-Oral Rush Desensitization to Mixed Cow and Sheep Milk: A Case Report

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Abstract

We attempted an oral rush desensitization with mixed cow and sheep milk in a 6-year-old boy who had had adverse reactions to cow and goat milks. Skin prick tests and specific immunoglobulin (Ig) E to cow, sheep and goat milks were positive. The double-blind, placebo-controlled food challenge with cow milk was positive too. He underwent a 12-day sublingual-oral desensitization treatment with mixed cow and sheep milk. Specific IgE and IgG4 were measured. Open oral challenges with cow milk, sheep milk and sheep cheeses were also performed after the desensitization. At the end of the desensitizing treatment our patient could tolerate 120 mL of mixed milk. Specific IgE levels did not vary, whereas an increase of specific IgG4 concentrations was observed. Open oral challenges with cow and sheep milks and sheep cheeses were negative. Oral rush desensitization may represent an alternative approach to the treatment of food allergy in children.

Resumen

Intentamos realizar una desensibilización rápida por vía oral con leche de vaca mezclada con leche de oveja, en un paciente de 6 años que había padecido reacciones adversas a la leche de vaca y de cabra. Se obtuvieron resultados positivos de las pruebas cutáneas y la inmunoglobulina (Ig) E específica a la leche de vaca, de oveja y de cabra. La prueba de provocación alimentaria con leche de vaca, doble ciego, controlada con placebo también fue positiva. Al paciente se le practicó un tratamiento de desensibilización oral sublingual de 12 días con leche de vaca mezclada con leche de oveja y se midieron la IgE e IgG4 específicas. Se realizaron pruebas de provocación oral abierta con leche de vaca y oveja y quesos de oveja después de la desensibilización. Al finalizar el tratamiento, nuestro paciente pudo tolerar 120 mL de leche mezclada. Las concentraciones de IgE específica no variaron, pero se observó un aumento de las concentraciones de IgG4 específica. Las pruebas de provocación oral abiertas con leche de vaca y oveja, y con quesos de oveja fueron negativas. La desensibilización rápida por vía oral puede ser una aproximación alternativa al tratamiento de la alergia alimentaria en niños.

Palabras clave: Alergia a la leche de vaca. Alergia a la leche de oveja. Alergia a la leche de cabra. Desensibilización rápida por vía oral.

Introduction

Spontaneous desensitization may occur in 19% to 44% of food allergic patients following an elimination diet, but this process takes years [1-3]. For those children who do not lose their food hypersensitivity, a desensitizing treatment should be taken into consideration. Oral or sublingual desensitization treatments for food allergy have been reported [4-10], but there are few studies concerning rush desensitization to foods [11-13].

Case Description

We studied a 6-year old boy suffering from atopic dermatitis and cow milk allergy. When he was 1 year old, he developed facial edema and dyspnea after drinking goat milk and at the age of 5 years he experienced edema of the lips and tongue itching after drinking cow milk.

The patient underwent skin prick tests with α-lactalbumin, ß-lactoglobulin and casein (Lofarma, Milan, Italy) and then with fresh cow, goat, and sheep milk (prick-to-prick).

Detection of total serum IgE (UniCAP, Pharmacia, Uppsala, Sweden), of specific IgE (UniCAP) and IgG4 (CAP FEIA, Pharmacia) to cow, sheep and goat milk allergens and of serum eosinophilic cationic protein (ECP) (UniCAP) was also performed with blood samples collected before the first dose of the desensitization protocol had been administered, just after the desensitization protocol was completed (at 12 days) and then at 1, 2, 4, and 24 months. A double-blind, placebo-controlled, food challenge (DBPCFC) was carried out on 3 successive days by administering placebo (soy milk flavored with vanillin) or cow milk (flavored with vanillin) after an interval of 3 days. Provocation was stopped if any adverse reaction was observed. After the DBPCFC, the patient was observed for 6 hours as described in detail elsewhere [9].

Four months after the positive DBPCFC, our patient underwent a specific sublingual-oral rush desensitization in hospital over a period of 12 days using mixed milk (50% cow milk and 50% sheep milk). The treatment was administered from 1 up to 6 times a day 20 minutes apart, sublingually in the first 4 days and orally on the subsequent days (Table 1). At the end of the desensitization protocol, the patient underwent further open oral challenges with sheep milk, cow milk, ricotta (a fresh Italian sheep cheese), and pecorino (a ripe Italian sheep cheese).

At the beginning skin prick tests were positive with α-lactalbumin, ß-lactoglobulin, casein, and with fresh cow, sheep and goat milks; tests for specific IgE to cow, sheep and goat milks and to milk proteins were also positive (Table 2). The DBPCFC with cow milk was positive (throat itching, facial erythema and edema of the lips after a dose of 20 mL at a cumulative dose 40 mL). Symptoms promptly remitted after oral administration of 5 mg of loratadine.

On the fifth day of the protocol, at the 3-mL dose, the patient experienced mild angioedema of the lips which disappeared spontaneously; so we decided to continue the oral desensitization by administering an oral antihistamine (loratadine 5 mg/day) 20 minutes before milk intake. Loratadine was interrupted at the end of the rush protocol (at the 12th day).

Specific IgE to ß-lactoglobulin turned negative after 4 months, while specific IgE to casein and goat milk decreased and specific IgE to α-lactalbumin increased. No other modifications of specific IgE levels were observed. After 24 months, specific IgE levels were significantly lower, especially those to cow, sheep and goat milks, and to casein and sheep milk whey (Table 2). On the other hand, specific IgG4 to all the studied allergens increased considerably at the end of the rush protocol (>30 000 µg/mL) after 1, 2, 4, and 24 months (Table 2).

When the desensitization was completed, open oral challenges with mixed cow and sheep milk, and cow and sheep milks by themselves were performed without loratadine administration. The patient was able to tolerate 120 mL of each and ate 100 g of ricotta and 50 g of pecorino cheese with no side-effects at all. After 2 years, the boy was drinking both cow and sheep milk and eating dairy products such as goat cheese and sheep cheese with no allergy symptoms.

Table 1. Protocol for Specific Sublingual-Oral Rush Desensitization (50% Cow Milk Plus 50% Sheep Milk)

Day	Dilution	Doses	Final Daily Amount of Undiluted Milk
1	10 drops of mixed milk in 100 mL of water	1 drop 3 drops 7 drops 12 drops 20 drops 30 drops	0.0064 mL
2	10 drops of mixed milk in 10 mL of water	1 drop 3 drops 7 drops 12 drops 20 drops 30 drops	0.064 mL
3	100 drops of mixed milk in 10 mL of water	1 drop 3 drops 7 drops 12 drops 20 drops 30 drops	0.64 mL
4		1 drop 2 drops 3 drops 4 drops 8 drops 12 drops	1 mL
5		0.5 mL 1 mL 1.5 mL 3 mL	6 mL
6		1 mL 2 mL 3 mL 4 mL	10 mL
7	Pure mixed milk	2 mL 3 mL 4 mL 5 mL 6 mL	20 mL
8		4 mL 6 mL 8 mL 10 mL 12 mL	40 mL
9		8 mL 10 mL 14 mL 18 mL 20 mL	70 mL
10		15 mL 25 mL 30 mL 50 mL	120 mL
11		40 mL 80 mL	120 mL
12		120 mL	120 mL

Table 2. Modifications of Total and Specific IgE, Specific IgG4 and IgA, and ECP During Sublingual Oral Rush Desensitization to Mixed Milk

	Start	End of Rush Desensitization	After 1 Month	After 2 Months	After 4 Months	After 2 Years
Specific IgE, kU/L						
Cow milk	26.3	34.3	38.9	41.6	38.8	8.40
Sheep milk	15.6	21.6	18.6	16.6	16.6	3.27
Goat milk	14.4	19.6	14.0	11.8	10.6	2.12
α-lactalbumin	7.88	10.7	8.95	9.27	11.5	4.65
ß-lactoglobulin	1.23	0.96	0.43	<0.35	<0.35	0.69
Casein	20.0	28.3	23.5	10.2	10.1	2.05
Sheep milk whey	13.5	18.1	12.2	12.6	12.3	2.64
Specific IgG4, µg/L						
Sheep milk	3438	6078	>30 000	>30 000	>30 000	>30 000
Goat milk	6072	9129	>30 000	>30 000	>30 000	>30 000
α-lactalbumin	818	2900	10 971	28 682	>30 000	>30 000
ß-lactoglobulin	205	904	2849	6101	8513	24 600
Casein	5702	9115	>30 000	>30 000	>30 000	>30 000
Sheep milk whey	4571	6251	29 812	27 019	>30 000	>30 000
Specific IgA, mg/L						
Cow milk	24.7	24.8	27.2	19.4	21.9	32.8
α-lactalbumin	<1.00	<1.00	<1.00	<1.00	1.44	<1.00
ß-lactoglobulin	<1.00	<1.00	<1.00	<1.00	<1.00	<1.00
Casein	<1.00	<1.00	<1.00	1.36	1.65	<1.00
Total IgEm kU/L	800	1075	911	963	1625	1357
ECP, µg/L	42.9	39.3	60.7	73.9	48.5	144

Abbreviations: ECP, eosinophilic cationic protein; Ig, immunoglobulin.

Discussion

In our previous reports we showed the results of a standardized protocol for oral desensitization with various foods, especially with milk, egg, codfish, wheat, and peanut [4-9,11]. However, there are a few reports in the literature that describe sublingual-oral rush desensitization treatment for food allergy. Poisson et al [12] obtained incomplete results with such a protocol because of the appearance of severe allergic reactions, and because the patient did not achieve full tolerance to milk. Bauer et al [13] successfully reached the dose of 200 mL of whole milk in 5 days but they did not use a DBPCFC to confirm the initial diagnosis [13]. We developed a new protocol for oral rush desensitization to mixed cow and sheep milks.

DBPCFC with sheep and goat milks were not performed in our patient because it has been shown that patients allergic to cow milk often react to goat and sheep milks because they are mainly sensitized to whey proteins and/or to the casein fraction [14]. Moreover our patient had a convincing history of goat milk allergy, positive skin prick tests, and high titers of specific IgE to sheep milk and whey.

The oral rush desensitizing treatment was performed using a mixture of 50% cow milk and 50% sheep milk because of the high cross-reactivity between sheep and goat milks. We had already observed that some patients with cow milk allergy, who successfully underwent an oral desensitizing treatment with cow milk alone are unable to tolerate sheep milk products (data not published).

During the DBPCFC our patient reacted to a 20-mL dose of cow milk, whereas during the desensitization protocol he reacted with 3 mL. This may be explained by the fact that we used mixed cow and sheep milk and that the latter contains higher amounts of allergen than the former [14].

Antihistamines are useful to prevent adverse reactions during oral desensitization and did not seem to modify the result of the protocol.

In our rush protocol it took 12 days to reach the dose of 120 mL of mixed milk because of the high levels of specific IgE at the beginning (Table 2) and the very low threshold dose.

The increase in specific IgG4 and the decrease in specific IgE levels are suggestive of a switch from a type 2 to a type 1 T-cell response [6]. Specific IgA to milk proteins in serum did not change and so they do not seem to play a role in the oral tolerance induction process. Total IgE and serum ECP remained high during the treatment probably because the patient suffered from atopic dermatitis (Table 2).

Sublingual-oral rush desensitization enabled the patient to achieve food tolerance in a shorter period than he would have with a traditional desensitizing treatment. This kind of treatment could be taken into consideration in food-allergic

patients who are at risk of allergen exposure. It should always be performed in a hospital setting and a fully equipped and trained team is necessary in order to treat possible anaphylactic reactions.

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