

Letter

SEVERE ALLERGIC REACTION TO LACTULOSE IN A CHILD WITH MILK ALLERGY

In this report, we describe a child who presented with dry cough and wheezing associated with ingestion of lactulose syrup for the treatment of constipation. A 4-year-old boy with severe milk allergy and atopic dermatitis since the first month of life was exclusively breastfed for 6 months. During breastfeeding his skin conditions improved markedly after strict avoidance of egg and milk in the mother's diet. After the child was weaned, the incidental ingestion of ricotta cheese was associated with vomit and urticaria-angioedema. The child successively presented with cough and wheezing associated with ingestion of boiled cow's milk. He did not tolerate extensively hydrolyzed casein formula (vomit, moderate urticaria, and cough after the ingestion of 50 mL), and consequently a soy formula was introduced in his diet at the age of 9 months. He presented successively with 3 episodes of anaphylaxis associated with the ingestion of hidden milk protein in different foods.

At the age of 30 months he was evaluated at our outpatient clinic for allergic diseases. Skin prick tests performed with commercial extract (Lofarma SPA, Milan, Italy) induced mean wheal diameters of 10 mm for milk, 7.5 mm for casein, 5 mm for egg white, 4 mm for histamine, and 0 mm for glycerinated saline. Positive reactions were also found to peanuts and cod, both of which were subsequently tolerated. A prick by prick test performed with ricotta cheese and freshly cooked cod was associated not only with a local reaction (a wheal mean diameter of 10 mm for both the foods) but also with the appearance within a few minutes of nasal itching and watery secretions, dry cough, and wheezing that required treatment with cetirizine and albuterol. This treatment was associated with prompt relief of signs and symptoms.

Serum specific IgE measured with the Pharmacia CAP System (Pharmacia Diagnostics, Uppsala, Sweden) resulted in levels greater than 100 kU/L for both milk and casein, 27.7 kU/L for egg, and 15.04 kU/L for cod. Mild positivity was also found for *Parietaria* and grass pollens.

At the age of 4 years, lactulose syrup (Laevolac) was prescribed for the treatment of constipation, and this was associated with the onset of dry cough that the mother reported to remind her the cough was associated with "asthma attacks." No other symptom or sign was reported by the mother. The child was then brought to our attention with the specific concern of a possible cause-effect relationship between lactulose administration and coughing.

A single-blind challenge with the syrup masked in soy milk was then performed. After a total of 2 mL of lactulose, the child experienced oral itching, diffuse erythema with conjunctival hyperemia, sneezing, and coughing suddenly followed by wheezing. There was no decrease in blood pressure, but heart rate increased to 140/min and respiratory rate increased to 45/min. The child was treated with

cetirizine and several puffs of albuterol. Signs and symptoms completely disappeared after 3 hours.

The ingredient list of the Laevolac brand of lactulose syrup used by the patient declares that the preparation contains pure lactulose (66.7 g/100 mL), potassium sorbate, and water. Bibliographic research disclosed that lactulose is prepared from lactose and supplied for clinical use as a flavored syrup containing approximately 50% lactulose, together with smaller amounts of galactose and of unchanged lactose (approximately 7 g of each per 100 mL).¹ Lactose is obtained from cow's milk after precipitation of casein with diluted hydrochloric acid, coagulation of albumins by heating (93.5°C), and finally purification by filtering.² This sugar is frequently included as an inactive component in many pharmaceutical formulations, including suspensions and tablets, without cautioning patients with milk allergy about the possibility of an allergic reaction to milk proteins, which may contaminate the lactose fraction.

A severe allergic reaction was previously described in a cow's milk allergic asthmatic child using a dry powder inhaler with lactose contaminated with milk proteins,³ but an allergic reaction to lactulose was never reported.

Allergenicity of milk proteins may be increased by formation of large lactose-protein complexes during the heating phase of lactulose extraction,⁴ which may explain the onset of the reaction even in the presence of a minimal quantity of proteins in sensitive patients. It would have been of interest to analyze the implicated lactulose preparation for its milk protein content, but this could not be done.

In conclusion, even though it has been reported that cow's milk allergic children can tolerate lactose-containing products,⁵ it is important to be aware that lactose is present in lactulose preparation, and if contaminated with milk proteins it may cause an allergic reaction in children with severe cow's milk sensitivity.

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