

REGULAR ARTICLE

Cow's milk allergic children can present sensitisation to probiotics

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Abstract

Aim: To evaluate sensitivity to different probiotics in children with cow's milk allergy.

Methods: Eighty-five patients (age range: 4 months–12 years) presenting atopic dermatitis (AD) were enrolled. Skin prick test (SPT) responses to three different probiotics preparations (Fiorilac®, Dicoflor® and Reuterin®) were evaluated in addition to relevant food allergens.

Results: Thirty-nine patients out of 85 (45.8%) had a positive skin response to prick test for cow's milk (3 with reaction <3 mm). Of the thirty-six patients with a cow's milk wheal reaction >3 mm, twenty-eight (77.8%) had a skin response to Fiorilac®, four patients (11%) to Dicoflor® and four (11%) to Reuterin®. The proportion of SPT reaction to all the investigated probiotics preparations was significantly lower than cow's milk ($r = 9.406$; $p = 0.002$). A significantly higher sensitization was observed for Fiorilac® versus Dicoflor® ($r = 30.916$; $p < 0.001$) and versus Reuterin® ($r = 34.133$; $p < 0.001$).

Conclusion: Probiotic use in patients with cow's milk allergy has to be limited to products that do not contain milk. This should be clearly reported in the label. In selected patients, it is advisable to perform a screening SPT with the product to evaluate its potential contamination with milk.

INTRODUCTION

A probiotic is a product with a sufficient number of viable microorganisms to alter the host's microflora to produce beneficial health effects (1). The criteria for a probiotic include that the strain be of human origin, that it be safe for human use and stable against acid and bile and that it adhere to the intestinal mucosa (2). Probiotics have been shown to alleviate intestinal inflammation, to promote gut barrier functions and to normalize altered gut microecology (3). Moreover, they may efficiently stimulate gut immune responses (4) and for this reason probiotics have been advocated for the prevention and treatment of AD (5–7), a disease frequently associated with food allergy in children (8,9).

However, it has been reported that not all probiotics can be safely used in children with cow's milk sensitivity (10,11). The finding of a breast-fed, 6 months old girl, sensitive to egg and cow's milk, with AD, which improved after avoidance of these foods in the maternal diet and worsened one day after the introduction of a probiotic preparation (Fiorilac®) to which she had a positive skin prick test (mean wheal diameter 5 mm), prompted us to perform a study on sensitization to different probiotic preparations in children with AD.

PATIENTS, MATERIALS AND METHODS

Eighty-five consecutive children (mean age 3.2 years, range 4 months–12 years) affected by atopic dermatitis, classified in accordance with the British Working Party (12) and with elevated risk for cow's milk allergy were enrolled into the study. Skin prick test (SPT) response to three different probiotic preparations available in our country (Fiorilac®, Pharmaland SA, San Marino; Dicoflor®, Dicofarm SpA, Rome,

Italy and Reuterin®, Noos srl, Rome, Italy) was evaluated in addition to the reaction to relevant food allergens, including cow's milk. SPTs were performed on the anterior surface of upper arm using a conventional lancets (Prick-test lancets Dome-Hollister-Stier®, Bayer, UK) according with the standard technique utilizing histamine for positive control and glicerococa for negative control.

Fiorilac® sachet (2 g) is a mixture of probiotics containing *Lactobacillus paracasei* I 1688 and *Lactobacillus salivarius* I 1794 (12:1) in doses varying from 0.1×10^9 to 10×10^9 and B₁ (0.6 mg) and B₂ (0.5 mg) vitamins. Dicoflor® 30 sachet (2.23 g) is composed by *Lactobacillus GG* in a concentration of 3×10^9 . Reuterin® is available in solution and 5 drops contain 10^8 CFU of *Lactobacillus reuteri*.

For SPTs, Fiorilac® sachet (2 g) and Dicoflor® were diluted in 10 mL of water, while 1 drop of Reuterin® was used without dilution. Reactions were evaluated 15 min later. Mean wheal dimensions were calculated by measuring major diameter plus its perpendicular diameter and dividing by two. All the wheal mean diameters were measured. However, only a wheal response 3 mm greater than the negative control was considered as a positive reaction.

STATISTICAL ANALYSIS

Data are given as mean $\pm$ SEM and Student's *t*-test was used to assess inter-group differences. Between-groups comparison for SPT response to the different probiotics was performed by chi-square test only for patients with a mean wheal size ≥ 3 mm. The linear correlation test was used to assess the relationship between the magnitude of SPT response (wheal diameters) to cow's milk and to the different probiotics.

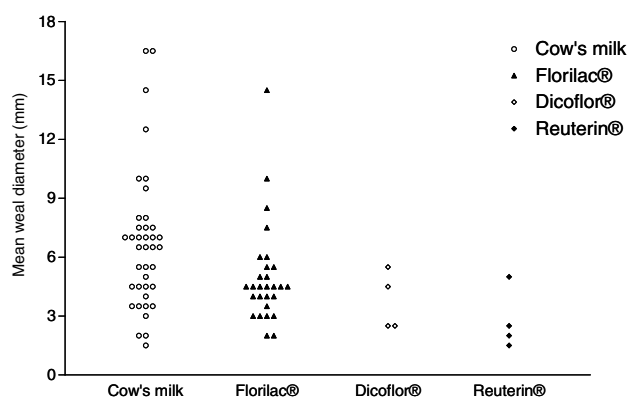


Figure 1 Mean wheal skin prick test diameter for different probiotics in children with cow's milk sensitization.

Approval for the study was obtained from the Hospital Committee and informed consent was obtained from children's parents.

RESULTS

SPT for cow's milk resulted negative (no wheal) in 46 children. Among these subjects, none had a wheal response to Dicoflor®, one patient showed a wheal response to Fiorilac® and one child to Reuterin®, both with a mean wheal diameter <3 mm.

Individual SPT response in subjects with any positive reaction to cow's milk is depicted in Figure 1. Thirty-nine patients out of 85 had a positive response to prick test for cow's milk. In three of these children the wheal was <3 mm and two of these patients presented a modest (<3 mm) reaction to Fiorilac®, but not to the other probiotics. Of the thirty-six patients with a cow's milk wheal size ≥ 3 mm., twenty-eight also tested positive to Fiorilac® (two children with a mean wheal diameter <3 mm), four patients to Dicoflor® (two children with a mean wheal diameter <3 mm) and four to Reuterin® (three children with a mean wheal diameter <3 mm). Thus, the prevalence of SPT reaction to milk was 42.3% in the entire study population. Among those with a positive reaction to cow's milk a positive response was observed in 72.2%, 5.5% and 2.8%, respectively for Fiorilac®, Dicoflor®, Reuterin®.

The proportion of SPT positive reaction to all the investigated probiotics was significantly lower than that for cow's milk ($r = 9.406$; $p = 0.002$). A significantly higher sensitization was observed for Fiorilac® versus Dicoflor® ($r = 30.916$; $p < 0.001$) and versus Reuterin® ($r = 34.133$; $p < 0.001$).

A linear correlation was observed between mean wheal diameter for cow's milk and Fiorilac®. ($r = 0.66$, $p < 0.001$).

DISCUSSION

There is a growing interest in the potential health-promoting benefits of probiotics in products that are now used every day in many countries by consumers in both clinical practice and in daily life (13, 14). Probiotics can be used to prevent

antibiotic associated diarrhoea (15) and they appear to be a useful adjunct to rehydration therapy in acute infectious diarrhoea (16) and in improving response to bacterial immunization (17). Probiotics have recently been advocated for the prevention and treatment of allergic diseases (5–7, 18). Probiotic bacteria may promote endogenous barrier mechanisms in patients with food allergy, and by alleviating intestinal inflammation, may act as a useful tool in the prevention and treatment of food allergy (19). Some studies have shown that probiotics reduce the occurrence of AD (20). Others have demonstrated a reduction in the severity of signs and symptoms in these patients (3, 5, 6, 21, 22).

However, these studies are not exempt from criticisms related to both study design and interpretation of the data (23). Furthermore, other studies have shown that probiotic supplementation has no significant impact on the symptoms of infantile AD (24) and that it might increase the risk of allergen sensitization in children with a high-risk of atopic diseases (25) and may be unsafe in subjects with cow's milk allergy (10, 11).

The results of our study confirm this last finding at least with some bacterial preparations. Probiotics are different from each other and some of them contain residual cow's milk allergens (10, 11).

Our study indicates that milk proteins, declared to be contained in the Fiorilac® preparation, are present in a sufficient amounts to elicit a positive SPT response in cow's milk-sensitized children. In four children the mean diameter of the SPT wheal with Fiorilac® was greater than the predictive cut-off index of positive response to oral challenge (>6 mm for children younger than 2 year old and >8 mm for older patients) (26). Even though we did not include oral challenge in our study it is tempting to speculate that the eventual use of this specific preparation might have induced worsening of AD symptoms in these children similar to what we observed in the patient who induced us to initiate this study. The content labeling does not always go with all probiotics (10,11) and the new European Food Labeling Legislation (27) may induce suppliers to adopt the easy option of a 'may contain' warning that can be a nightmare for allergy sufferers (28). In the specific case of Fiorilac®, the manufacturer has decided to modify the formulation of the product with a milk-free preparation (personal communication).

In conclusion, since cow's milk allergy is one of the most common food allergies in infants with an incidence of 2% to 3% in the first year of life (29), the use of probiotics in these patients has to be limited to the products which do not contain food allergens and this should be clearly reported on the label. If this is not the case and there are the clinical indications for the use of probiotics, in high-risk children, it is advisable to perform a screening SPT with the product to evaluate contamination with allergens.

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