

SHORT COMMUNICATION

Increased concentration of fecal α_1 -antitrypsin is associated with cow's milk allergy in infants with atopic eczema

H. MAJAMAA*†, J. AITTONIEMI‡ and A. MIETTINEN‡

*Medical School, University of Tampere, †Department of Dermatology and ‡Centre for Laboratory Medicine, Tampere University Hospital, Tampere, Finland

Summary

Background The use of fecal α_1 -antitrypsin in the monitoring of intestinal inflammation in infants with atopic eczema and food allergy was evaluated.

Methods The study material comprised 26 atopic infants with confirmed food allergy. Fecal samples were collected before an elimination diet and 3 months later for the determination of α_1 -antitrypsin.

Results Nine (35%) of the 26 patients demonstrated an increased fecal concentration of α_1 -antitrypsin (median 3 mg/g; range 2.8–6.4 mg/g). In all nine patients (100%) the oral cow's milk challenge was positive as opposed to only six (35%) in those with normal α_1 -antitrypsin concentration ($P = 0.0024$). No further connections between α_1 -antitrypsin and other food allergies were detected. As a result of an adequate elimination diet, the fecal concentration of α_1 -antitrypsin was normalized in seven patients, with a favourable clinical response in atopic eczema in six and no improvement in one patient.

Conclusions Our results indicate that serial determinations of fecal α_1 -antitrypsin provide a useful non-invasive tool for the detection and follow-up of intestinal inflammation in a certain group of atopic infants with cow's milk allergy and severe inflammation of the gut.

Keywords: α_1 -antitrypsin, intestinal inflammation, food allergy, atopic eczema

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Introduction

Food allergy is a common problem in infants and small children. It develops as a result of interaction between food allergens and the immune system of the gastrointestinal tract and usually manifests as atopic eczema [1,2]. It has recently been shown that these patients also present with intestinal inflammation [3–6].

α_1 -Antitrypsin is an acute phase serum protein and a protease inhibitor secreted by the liver. In inflammatory bowel disorders associated with abnormal protein loss, α_1 -antitrypsin leaks to the lumen of the gut, and its determination is a valuable screening test for these conditions [7].

The aim of the present study was to evaluate the use of fecal α_1 -antitrypsin in monitoring intestinal inflammation in infants with atopic eczema and food allergy.

Materials and methods

The study material consisted of 26 infants (eight girls, 18 boys), median age 7 months, range 5–16 months. They had been admitted to the Department of Dermatology, Tampere University Hospital, because of atopic eczema and suspected food allergy. Infants with atopic eczema and confirmed allergy to egg, cow's milk and/or cereals were included in the study [3]. Six patients were manifesting both atopic eczema and gastrointestinal symptoms, such as loose stools or diarrhoea. Nutritional status was normal in all infants.

Correspondence: Heli Majamaa, Department of Dermatology, Tampere University Hospital, PO Box 2000, FIN-33521 Tampere, Finland.

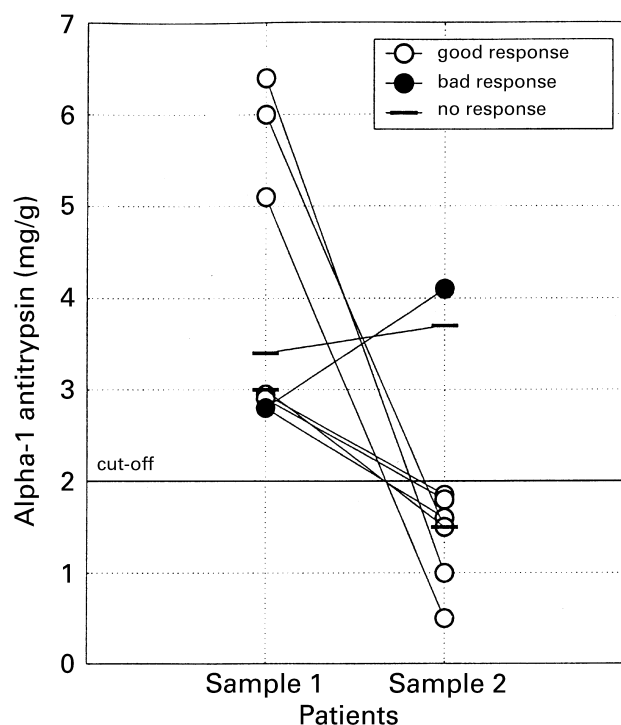


Fig. 1. Changes observed in elevated fecal α ₁-antitrypsin concentrations during an elimination diet in atopic infants with food allergy. In those infants with good response to the elimination diet, the decrease in α ₁-antitrypsin concentration was statistically significant ($n = 6$, $P = 0.028$).

Total serum concentration of immunoglobulin E (IgE), specific IgE antibodies by RAST and skin prick tests for various foods were determined on the first visit to the hospital as previously described [8]. On the basis of a positive skin prick test or RAST and anamnestic data the patients were put on an elimination diet, excluding offending foods. Later, oral double-blind food challenge with cow's milk and/or wheat was done as previously described [9,10] to confirm food allergy diagnosis. Egg allergy confirmed by positive skin prick test or RAST was found in 20 infants. All patients were seen by the same physician (H.M.) at the beginning and at follow-up visits. A clinically evident amelioration of atopic eczema was defined as a good response.

Fecal samples were collected before the onset of an elimination diet and approximately 3 months later for the determination of α ₁-antitrypsin. The quantitative determination of α ₁-antitrypsin in faeces was performed as previously described [3]. The concentrations of α ₁-antitrypsin were given as mg/g dry weight of faeces. Fecal concentrations of α ₁-antitrypsin below 2 mg/g were regarded as normal, based on observations in healthy infants [3]. Fisher's exact, Mann-Whitney U, and Wilcoxon matched pairs tests were used in statistical comparisons.

Results

Before the onset of the elimination diet, nine (35%) of the 26 patients demonstrated increased fecal concentrations of α ₁-antitrypsin (median 3 mg/g; range 2.8–6.4 mg/g). The oral cow's milk challenge was positive in all nine patients (100%) as opposed to only six (35%) of those with a normal level of α ₁-antitrypsin ($P = 0.0024$). Furthermore, in three of those six with a normal level of α ₁-antitrypsin, cow's milk had already been eliminated from the diet in primary health care a few months earlier on the basis of clinical suspicion of cow's milk allergy. No further connections between α ₁-antitrypsin and other food allergies or laboratory parameters were detected.

The changes observed in the elevated fecal α ₁-antitrypsin concentrations during the elimination diet are illustrated in Fig. 1. The α ₁-antitrypsin concentration was normalized in seven of the nine patients with elevated fecal concentrations. Six of these also showed a favourable clinical response in atopic eczema, and the decrease in α ₁-antitrypsin concentration was statistically significant ($P = 0.027$). In one patient, no improvement was detected. In two patients the concentration of α ₁-antitrypsin remained elevated despite the diet. In one of them the clinical status did not improve and in the other it deteriorated. In the latter patient, new food allergens were found and eliminated from the diet on the follow-up visit.

Discussion

Food allergy makes an important contribution to the pathogenesis of atopic eczema in infants [3,6,9–12]. However, surprisingly little is known about the possible coexistence of intestinal inflammation. We have previously demonstrated the importance of elevated fecal concentrations of tumour necrosis factor- α , eosinophil cationic protein, and eosinophil protein X as indicators of intestinal inflammation in infants with atopic eczema and food allergy [3,5,6]. Increased numbers of eosinophils have earlier been found in the duodenal mucosa of patients with cow's milk allergy [4].

The determination of fecal α ₁-antitrypsin has been suggested to be useful in identifying patients with inflammatory bowel disorders [13,14]. In this study, increased fecal concentrations of α ₁-antitrypsin were observed in 35% of atopic infants and it was strongly associated with cow's milk allergy. This finding implies a connection between elevated α ₁-antitrypsin level and severe chronic inflammation of the gut due to extensive exposure of allergic infants to cow's milk antigens [15,16].

As a result of an adequate elimination diet, the elevated fecal concentration of α ₁-antitrypsin returned to normal in the majority of the atopic infants with food allergy. The

decrease was associated with improvement in atopic eczema, thus implying diminished intestinal inflammation.

In conclusion, serial determinations of fecal α_1 -antitrypsin provide a useful non-invasive tool for the detection and follow-up of intestinal inflammation in a certain group of atopic infants with cow's milk allergy and severe chronic inflammation of the gut.

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