

further testing with TMP and SMX separately. Patient 2 exhibited a positive reaction to cotrimoxazole in lesional skin of the right flank, and to SMX, but not to TMP, in residual lesions of the left flank. The tests became positive 2 h after they were performed, and they were negative in the control areas.

■ Provocation tests showed good tolerance of Optalidón in patient 1 and of lysine acetylsalicylate in patient 2.

■ Patch testing on previously affected skin has given variable results in FDE (1), especially with

*Lesional skin testing seems to be an improved approach to the diagnosis of trimethoprim-sulfamethoxazole-induced fixed drug eruption.*

trimethoprim and sulfonamides (2); this may be related to the fact that the best concentration and vehicle for each drug have yet to be found (3). The diagnosis of FDE can be established by oral challenge, an approach that may involve risk (4). Improvement in diagnostic accuracy has

been reported with intradermal tests in some cases of drug-induced allergic contact dermatitis (5, 6), but these tests have only occasionally been used for FDE diagnosis. Positive intradermal results have been reported in FDE caused by antipyrine and alurate, although negative results were obtained with phenolphthalein (7). We have found no reports of intradermal tests in the diagnosis of FDE due to cotrimoxazole. The positive results of the intradermal tests with negative lesional patch tests may be explained by better absorption. This procedure causes minimum discomfort, and, in our patients, no generalized reactions have developed. In fact, the only apparent drawbacks of this test are 1) the lack of soluble preparations of the drug, and 2) mucosal FDE, without cutaneous involvement.

Patient 2 reported good tolerance of cotrimoxazole between the two last episodes. This seems to correspond to the refractory period described by some authors (8), which has not previously been reported for cotrimoxazole. A refractory state could explain, in some cases, the negative results of lesional patch tests. In our cases, the tests were performed 6 (patient 1) and 3 months (patient 2) after the last episode. Patch and intradermal tests were simultaneously performed in patient 1 and after a 48-h interval in patient 2; therefore, a

hypothetic refractory state does not explain our results.

In case 1, two of the most frequently reported FDE-eliciting agents (9) were involved. In case 2, the severity of the eruption was increasing. If we had performed only patch tests, an oral challenge would have been necessary to establish a diagnosis. In our cases, the lesional intradermal test has been safe, easy to perform, and useful.

Key words: cotrimoxazole; drug reactions; fixed drug eruption; lesional intradermal tests; sulfamethoxazole; trimethoprim.

J. A. NAVARRO\*, M. T. AUDÍCAN, F. VILLAS, A. JORAL, J. GARMENDIA, D. MUÑOZ, J. ZUBIZARRETA

\*Hospital de Amara

Paseo del Dr. Beguiristáin, 107

E 20014 San Sebastián

Spain

Tel. 34-43-451922

Fax: 34-43-471922

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## Copro-eosinophil cationic protein (ECP) in food allergy

THE EUROPEAN Academy of Allergology and Clinical Immunology subcommittee has concluded that diagnosis of food allergy must be based on the demonstration of clinical intolerance of a given food by a double-blind, placebo-controlled food challenge (DBPCFC) (1). We earlier reported good results from the measurement of copro-IgE (2). In the present study, we have investigated the correlation between the serum and copro-ECP levels. The serum and copro-ECP levels were examined before the start of an allergen-free diet, during

the diet, during the oral challenge, and after the challenge.

■ Fourteen children (nine boys and five girls) with food allergy were investigated. The youngest child was 5 months old and the eldest 13 years. Their allergic status was proved by means of serum and coproallergen-specific IgE and oral challenge. The children suffered from cow's milk, hen's egg, or soybean allergy. Six of the children had wheezy bronchitis and atopic dermatitis, six atopic dermatitis, and two enteritis and atopic dermatitis. After admission, copro- and serum samples were taken for ECP-level measurement and an allergen-free diet was started. After 24 days on this allergen-free diet, the copro- and serum ECP level were measured again.  $\alpha$ -1-Antitrypsin ( $\alpha$ 1-AT) levels were also

*Measurement of ECP  
in feces of children may  
prove useful in diagnosis  
and monitoring of  
food allergy  
and effect of diet.*

measured in all children. On the next day, the children aged above 3 years underwent DBPCFC, while those under 3 years underwent a simpler method because of the risk of an anaphylactic reaction. The provocation test

lasted 2 days, and the quantity of allergen was gradually increased; in the event of an adverse reaction, the challenge was stopped.

ECP levels were measured with the Pharmacia CAP System (Pharmacia, Uppsala, Sweden) and Pharmacia ECP kits.  $\alpha$ -1-Antitrypsin was measured by the Orion nephelometer.

Feces were prepared by the method of Kollmannskog et al. (3).

Fisher's exact test was used to compare intergroup differences in parameters.

■ Table 1 shows the copro- and serum ECP levels before the diet, during the diet, during the challenge, and after the challenge. The values before the diet did not significantly differ from those after the challenge ( $P > 0.1$ ). Similarly, there was no significant difference ( $P = 0.5$ ) between the ECP level

during the diet and that during the provocation test. However, there was a significant difference ( $P < 0.001$ ) between the results before the diet or after the challenge and those during the diet or during the challenge. The levels before the diet and after the provocation test were significantly higher than the levels during the diet and during the challenge ( $P < 0.001$ ). Like the copro-ECP levels, significantly higher serum-ECP values were observed before the diet or after the challenge than during the diet or during the provocation test ( $P < 0.01$ ). The copro-ECP level was significantly higher than the serum-ECP level at all stages of the study ( $P < 0.001$ ).

The presence of the symptoms in the challenge test exhibited a close correlation with the copro-ECP levels. During the provocation test, no serious adverse reaction was observed. Mild symptoms were treated immediately. At the completion of the examination, all 14 children were kept on the diet and they became symptom-free.

Food allergies are always problematic for parents and specialists. Establishment of the correct diagnosis usually takes a long time in the hospital. Moreover, the original factors often cannot be discovered. A correct diagnosis is especially rare for food allergies because of the various immunologic mechanisms (4). IgE-mediated food allergy can be proved by allergen-specific IgE and DBPCFC. In some cases, the antigen level is too low to be measured. The eosinophils and their derivatives play a very important role in various allergic inflammations (5). The level of ECP (one of the most important proteins in eosinophils) can readily be measured. In addition, we have investigated  $\alpha$ -1-antitrypsin levels in fecal extracts in parallel with ECP. Therefore, it seems unlikely that ECP in the feces of food-allergic children is the result of simple diffusion from the blood. Accordingly, it is believed that an increase in copro-ECP levels represents a localized immune reaction after food-allergen stimulation of the gut mucosa. By Kollmannskog et al.'s method, we obtained samples from the place where the allergic reaction may develop, and these samples can be well prepared for the measuring of different mediators (3). This work studied the change of ECP level in serum and feces. Our data indicate that the ECP levels in the feces rise more significantly in response to a food challenge than those in the serum. It seems that the copro-ECP level shows better the local immunologic change than does the serum level. The measurement of ECP may prove useful not only in the diagnosis and monitoring of food allergy, but also in the evaluation of the diet, for which an objective parameter is needed to complement subjective clinical assessments.

Table 1. Mean copro- and serum ECP levels in children with food allergy

|                              | Before diet     | During diet     | During challenge | After challenge |
|------------------------------|-----------------|-----------------|------------------|-----------------|
| Copro-ECP<br>(mean $\pm$ SD) | 76.3 $\pm$ 29.8 | 32.4 $\pm$ 12.4 | 43 $\pm$ 20      | 83.3 $\pm$ 20.5 |
| Serum ECP<br>(mean $\pm$ SD) | 26.8 $\pm$ 13.4 | 17.9 $\pm$ 11.3 | 30.2 $\pm$ 8.6   | 33.2 $\pm$ 15.6 |

Key words: eosinophil cationic protein (ECP); food allergy; food challenge.

L. KÓSA\*, E. KEREKI, L. BÖRZSÖNYI

\*Children's Institute, Svábhegy (formerly Szabadsághegy)

Veterinary University

Budapest

Hungary

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