

SIT with a depigmented, polymerized mite extract

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Key words: Immunotherapy, *Dermatophagoides*, allergen vaccine, bronchial provocation, clinical efficacy.

• It has been shown that allergen specific immunotherapy produces clinical benefit in mite allergic patients (1). In most studies, the threshold dose eliciting an immediate bronchial obstruction following immunotherapy was increased significantly using specific bronchial challenges as an objective criterion of efficacy (1). To achieve this goal, a series of injections over a long period of time is required. The time needed to achieve efficacy can be shortened by the use of higher doses, although this approach is more dangerous since a relationship between the dose administered and the appearance of adverse effects has been established.

In an attempt to overcome this disadvantage, glutaraldehyde-modified allergenic extracts were developed, proving to be safer than unmodified vaccines while retaining their clinical efficacy (2,3). A further improved method, which includes, before polymerization, a depigmentation step in which the enzymatic activity is inactivated and the pigments are removed, has recently been developed. This process allows the administration of larger doses than of native extracts.

Thirty-three patients were included in an open, controlled and parallel study. All the patients met the following criteria: mild or moderate bronchial asthma of more than two years of evolution, and sensitized to *D. pteronyssinus* and *D. farinae*. The exclusion criteria were those outlined in the WHO position paper on allergen immunotherapy (1). They were randomly assigned to receive treatment with a mixture of *D. pteronyssinus* and *D. farinae* modified allergen vaccine (Depigoid[®], CBF LETI, S.A., Madrid, Spain)

(active group; $n=22$); or only pharmacological treatment (control group; $n=11$).

The modified extracts showed a decrease in overall IgE binding potency >95% when compared with the native unmodified extracts. The potency for human IgG-antibody binding remained without modification. The native extract of *D. pteronyssinus* contained 20.35 µg of Der p1 and 12.30 µg of Der p2 per mg of freeze-dried extract, and *D. farinae* contained 19 µg of Der f1. After the polymerization process, Der p1, Der p2 and Der f1 were not detectable in the modified extract. The active group received five injections of build up and six maintenance doses. The total number of injections was 232, and only four local reactions with a diameter > 10 cm were recorded.

Specific bronchial provocation test (BPT) was performed at baseline and after 6 months using native, standardized (in HEP units), unmodified extract of *D. pteronyssinus*. A significant difference in the amount of native extract of *D. pteronyssinus* needed to produce a drop of 20% in the FEV₁ ($p=0.0029$, Wilcoxon test) in the active group was found (median at baseline was 0.6 HEP (35 µg) vs. 3.96 HEP (232 µg) at the end), whereas no difference (median 0.6 vs. 0.57 HEP) was found in the control group.

After the treatment, 10 patients in the active group needed more than twice the amount of the native allergen to obtain a positive BPT, whereas only one did in the control group ($p=0.028$ by contingency table analysis).

The results demonstrate that the modified vaccine-treated patients experience a significant clinical improvement after only 6 months of treatment in the objective outcome of specific bronchial provocation test.

It is now accepted that an important feature of the efficacy of specific immunotherapy is the delivery of high doses of allergen. Commonly, monthly maintenance doses for mite immunotherapy ranges from 0.5 to 11.5 µg/ml (4–7). In the present study, the highest administered dose was 42.5 µg of freeze-dried modified extract of *D. pteronyssinus* and 32.5 µg

D. farinae. Therefore, the combined highest dose was 75 µg in 0.5 ml. These doses are the equivalent of chemically modifying 10 times the usual dose of a nonmodified extract. The total accumulated dose was 296.65 µg of modified extract of *D. pteronyssinus* and 226.85 µg of *D. farinae* (523.5 µg of total extract).

An important conclusion of this study is that the modified extract of *D. pteronyssinus* and *D. farinae* clearly protects against mite allergens present in the native extracts. It suggests that the clinically relevant epitopes are present in the polymer. These findings are in agreement with the specific IgG data, which demonstrates that both, native and polymer, retained IgG binding epitopes in the same proportion, while specific IgE binding epitopes were significantly reduced in the polymer.

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Occupational exposure to pectinase

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Key words: pectinase; proteolytic enzyme; sensitization.

● PROTEOLYTIC ENZYMES are used in many industrial processes, particularly in detergent production, the treatment of fruit, for agriculture, the baking industry, and wine-making. Enzyme allergy has been recognized since 1970; it can cause asthma, rhinoconjunctivitis, allergic contact dermatitis, and contact urticaria (1,2). The frequency of sensitization in exposed subjects has been reported at 4-60% (3), and the prevalence of respiratory disease 5-57% (2,4). Only three cases of allergic reaction due to pectinase were reported in the literature (5,6).

In the period between 1993 and 1999, 13 workers from a small factory selling pectinase and concentrated protopectinase came to the outpatient clinic of the Institute of Occupational Health of Brescia. Detailed work histories and information on work-related symptoms were collected for all the workers, who also underwent medical

**A potent sensitiser,
also of nonatopics.**

examination, respiratory function tests, chest X-rays, and measurement of total serum IgE and IgE antibody to pectinase (radioallergosorbent assay, RAST).

The subjects comprised seven men and six women, of mean age 39.2 years, with mean duration of employment of 9.5 years, and mean duration of exposure to pectinase of 4.3 years. Seven were smokers. Seven symptomatic workers referred latency of reaction, from the beginning of exposure to pectinase to the onset of dyspnoea and rhinitis, of between 4 and 24 months. No worker had any family history or personal history of atopy. Based on the clinical history (work-related symptoms 3/4 even past symptoms) and the results of allergologic tests, we diagnosed five cases of allergic occupational asthma, one of irritant occupational asthma, and one of irritant occupational rhinitis.

Among our population, the prevalence of sensitization to pectinase was 61%, while the prevalence of both sensitized and symptomatic subjects was 38%. These data are similar to those reported in studies on workers exposed to other proteolytic enzymes (2-4). No worker was atopic, which means that no workers had any family or personal history of past or present IgE-mediated allergic reactions to common allergens. In this population, the high frequency of sensitization and the short latency of the onset of work-related symptoms allow us to consider pectinase as a strong sensitizer, as are the other proteolytic enzymes (7).

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Do sex hormones influence airway mucosa?

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Key words: Asthma, sex hormones, estrogen, progesteron, and inflammation.

● In this study, we aimed to investigate the effects of sex hormones on bronchial tissues of mice.

Even though allergic mechanisms are of importance in about 80% of childhood asthma and in about 40-50% of the adult form, clinical observations and epidemiological studies show that the sex of the patient also may exert an important influence on the incidence, severity and progression of asthma (1). In early childhood wheezing and asthma are more common in boys than girls (2). In contrast, girls are more likely than boys to develop asthma in adolescence (3). In a new study, it is found

**No significant effects
were found on
bronchial epithelium of
mice**