

Occupational asthma in bakeries caused by sensitivity to α -amylase

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We report on a patient with asthma induced by occupational exposure to α -amylase derived from *Aspergillus oryzae*, which is a component of bread additives. A type I hypersensitivity to this enzyme was demonstrated by means of skin test, immunoassay for specific IgE, and immediate bronchial provocation test response to an α -amylase extract.

Key words: α -amylase; baker's asthma; occupational asthma.

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The existence of occupational asthma secondary to the inhalation of enzyme dusts has been described (2, 4, 5, 6, 8, 9, 11) in patients exposed to them during preparation for their later industrial use.

Our patient is a baker who developed occupational asthma caused by sensitivity to α -amylase, which is a component of a bread additive used to increase the quality of bread.

CASE REPORT

The patient was a 23 year-old man, a baker who experienced nasal and ocular itching, rhinorrhea, sneezing, shortness of breath and wheezing after 4 working years. When not at work his symptoms were significantly improved.

The bakery was 70 m² with four windows and three air extractors, and was thus well ventilated. During bread-making, apart from wheat and rye flour, he used a powder to improve its quality. This powder mainly contained soya flour and α -amylase (from *Aspergillus oryzae*). He worked with 150 kg flour every day, and used 200 mg powder (containing 3% α -amylase) to each 25 kg flour.

He had no personal or family history of other allergies.

The clinical examination was normal and there were no eosinophils in the white blood cell count. Chest X-ray was normal. The sputum contained 80% eosinophils. Spirometry was normal (FEV₁ was 94% of the predicted value).

Skin prick tests were done with a battery of commercially available allergens (Lab. Aristegui, Spain) which included *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Aspergillus fumigatus*, *A. niger*, *Mucor racemosus*, *Penicillium notatum*, *Cladosporium herbarum*, *Alternaria tenuis*, grass pollen mix, and danders. They were all negative. Total IgE was 750 IU/ml.

MATERIAL AND METHODS

Extracts. Five grams of wheat, rye and soya flour and α -amylase were individually incubated in 25 ml PBS for 18 h at 4°C with continuous stirring. After straining through filter paper the solution was passed through a millipore filter (0.22 micra). We made progressive dilutions up to 10⁻⁵ from the starting solution.

Skin prick tests were done with antigenic preparations described above. The positive control was histamine 10 mg/ml and the negative was PBS. Ten non-exposed subjects with asthma, and six exposed asymptomatic persons were also tested

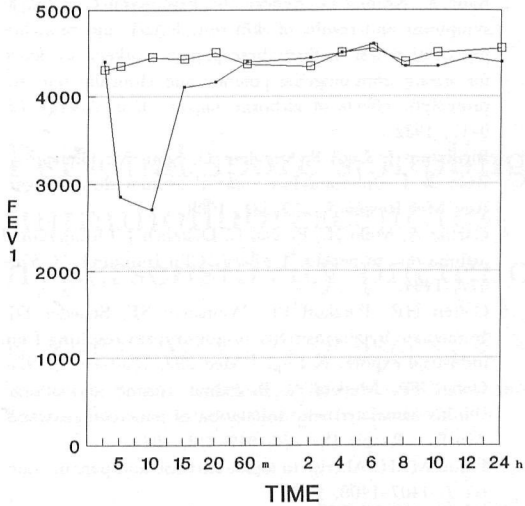


Fig. 1. Bronchial provocation test with alpha-amylase 1/10000.

as a control group. All skin tests were examined after 20 min and 6 h later.

Specific IgE antibody determination was performed by commercial immunoassay (Phadebas-Pharmacia, Uppsala, Sweden) to wheat, rye and soya flour, α -amylase and storage mites (*Lepydoglyphus destructor*, *Tyrophagus putrescentiae*, *A. siro*).

Bronchial provocation tests were always done during asymptomatic periods, and the patient received no medication at the time of the study. Vital capacity and FEV₁ were > 80% of the theoretical values.

For those substances in which skin and immunoassay tests were negative we performed bronchial provocation tests by inhalation of capsules containing lactose mixed with increasing powder doses (0.002 g to 0.128 g), fitted into a turboinhaler (Spinhaler, Fisons Corp, Bedford, Mass).

For those substances with positive skin prick and immunoassay tests, the bronchial provocation test was done by inhalation, using a De Villbis 646 with an input of 6 l/min and an output of 0.280 ml/min. The subject's nose was clipped and the solution delivered into a mask over the mouth and inhaled by tidal breathing for 2 min. Challenges were preceded by a control inhalation with PBS solution which caused no reaction. The starting

solution for the inhalation test was the dilution following the one which produced a wheal on the skin test which was 3 mm larger than the negative control. The extract was given in progressively increasing concentrations.

In both methods, the interval between doses was 20 min. FEV₁ and FVC were measured before and at intervals of 5, 10, 20, 30, 60 min 2, 4, 6, 8, 10, 12 and 24 h after the dose which produced a reaction or, the highest inhaled dose. Only one extract was used for provocation each day.

RESULTS

Skin prick tests with wheat, rye and soya flour extracts were negative. The skin prick test with α -amylase was negative to the dilution 10^{-5} . With 10^{-4} a 3 mm wheal for 5 of histamine was obtained. Higher concentrations of 10^{-3} , 10^{-2} and 10^{-1} , caused wheals of 5, 9, and 14 mm, respectively. There was no later reaction. None of the tested controls showed any skin reactions.

Specific IgE determination to α -amylase showed a 14.3 PRU level (grade 3 to the reference standard rate). It was negative for the rest of the allergens tested.

Bronchial provocation test produced no reaction after challenges with wheat, rye and soya flours. The inhalation of a 10^{-5} dilution of the starting α -amylase solution caused no significant changes in FEV₁ (a fall of 5%). Five minutes after inhaling a 10^{-4} dilution, the patient suffered shortness of breath and wheezing. A fall in FEV₁ of 31%, and in FVC of 22% was observed. No late reactions were noted (Fig. 1).

The patient could tolerate 10^{-4} and 10^{-3} dilutions after premedication with DSCG, but in spite of this the 10^{-2} dilution provoked a 25% fall in FEV₁.

DISCUSSION

Baker's asthma is a classic allergy. Various allergens have been reported in its etiology (10).

α -Amylase is a proteolytic enzyme that can be obtained from the pig pancreas, *Bacillus subtilis* or *Aspergillus oryzae*. It is mainly used in the pharmaceutical industry as an anti-inflammatory and digestive enzyme and, more recently, in the food

industry, being added routinely to baking flour to compensate for the low natural content of amylases and thus of carbohydrates fermentable by yeast. α -Amylase stimulates the growth of *Saccharomyces*, improving the rising of the dough and the quality of the bread.

We have only found two references in the literature that relate baker's asthma to α -amylase sensitivity (1, 3). In previous cases the patients worked with enzyme dusts in industries which produced these for later industrial use (7).

We have demonstrated in our patient, whose case is the first published in Spain, the immunologic mechanism implicated. Positive skin prick tests prove an immediate response. The presence of specific IgE in the patient's serum was demonstrated by immunoassay tests. The bronchial challenge test provoked an immediate response partially modified by pretreatment with DSCG. All these findings are consistent with a classic IgE antibody-mediated reaction. We have rejected, through similar tests, the possibility of other allergens having an effect on the patient's asthma.

We draw your attention to the role that components used to improve the quality of bread, and more specifically α -amylase, could act as etiologic agents responsible for sensitivity and the cause of baker's asthma.

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