

Asthma caused by bromelin inhalation

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(Received 23 June 1977; accepted for publication 9 August 1977)

Summary

Two cases are reported of bronchial asthma caused by inhalation of bromelin, a proteolytic enzyme utilized in some anti-inflammatory medicines.

Prick test results with bromelin extract were positive. Inhalation tests gave immediate reactions which were blocked by sodium cromoglycate, but not corticosteroids.

Introduction

Bromelins are a group of proteolytic enzymes extracted from the fruit and leaves of the pineapple (*Ananas comosus*). Clinically they have been used as anti-inflammatory agents or as digestive aids. They are capable of digesting casein and have fibrinolytic, mucolytic and bradykinin action.

We have examined two patients with asthma brought on by bromelin inhalation. The medical literature contains reports on asthma after inhalation of trypsin (Zweiman *et al.*, 1967) or enzymes derived from *Bacillus subtilis* (Gómez, 1970; Newhouse *et al.*, 1970; Zweiman *et al.*, 1967), but, as yet, we have found no such descriptions associated with the inhalation of bromelin.

Methods and results

Patients

Case 1. J.C.C., male, 22 years old, who had no history of previous illness. From June 1972 he suffered episodes of bronchial obstruction and rhinitis while working at a pharmaceutical laboratory preparing medicines, one of which contains bromelin.

He wore no protective clothes while working with the bromelin, and the dust inhalation was massive.

Spirometry revealed completely reversible airways obstruction. When he left his job, he had no further asthma crises. Prick tests to common allergens were all negative.

There was no asthma or rhinitis in the family history, and he was a non-smoker.

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Case 2. L.R.T., male, 28-years-old, who had no history of previous illness. He had episodes of bronchial obstruction for the past 4 years. He worked as messenger boy in a pharmaceutical laboratory, and associated his symptoms with inhalation of dust and proximity to the section where bromelin was processed. He reported having similar attacks after eating pineapple. In addition to bronchial obstruction, he had rhinitis and ocular itching, with red eyes. Prick test to *Dermatophagoides* sp. gave a positive reaction.

There was no asthma or rhinitis in the family history.

Prick tests

The enzymes were defatted overnight in ether, extracted in Coca's solution for 7 days and were filtered, dialysed and lyophilized.

Prick tests were made with this antigen at 10 mg/ml, on 100 asthma patients and seventy workers at one of the pharmaceutical laboratories.

The 100 asthma cases all gave negative reactions, and of the seventy workers, four gave positive reactions and two of them were asthmatic.

The two patients under study gave immediate reactions only, some 10 and 12 mm in diameter respectively.

Challenge tests

Using a single blind method, the patients were tested by inhalation of bromelin in 2% lactose, or by inhalation of pure lactose, for 10 min. They wore a gown and cap and were asked to pour the powder repeatedly from one tray to another. After 10 min, the gown and cap were removed and the patients were taken to another room so as to terminate the inhalation of the powder.

Basal FEV₁ was measured, and then at 1, 5, 10, 15, 30, 45 and 60 min, selecting the higher of two readings.

The patients were kept under observation for 8 hr and were examined the following day for a delayed reaction.

Patient 1 gave an immediate reaction, and a delayed reaction was suspected. The response was blocked by Intal, but not by corticosteroids (Fig. 1). The precipitin test was negative.

Patient 2 gave an immediate reaction, with rhinitis and reddened eyes (Fig. 2).

Discussion

Proteolytic enzymes are a special group of substances utilized for therapeutic purposes, and they are also added to detergents for everyday use, as in the case of enzymes derived from *Bacillus subtilis*.

Newhouse *et al.* (1970) studied workers in a factory processing alkalase, a proteolytic enzyme derived from *B. subtilis*. She found 21% positive reactions to prick tests with much more frequent reactions in the atopic cases. Flindt (1969) found type III asthmatic reactions in patients working in the preparation of enzymes derived from *Bacillus subtilis*.

It is well known that antigen sensitization is determined by three factors: (a) the immunological reactivity of the individual; (b) the antigen's ability to induce sensitization; and (c) the characteristics of the antigen exposure.

We could infer different sensitization mechanisms in our two patients. Case 1 is a non-atopic patient whose sensitization required massive and prolonged exposure to the

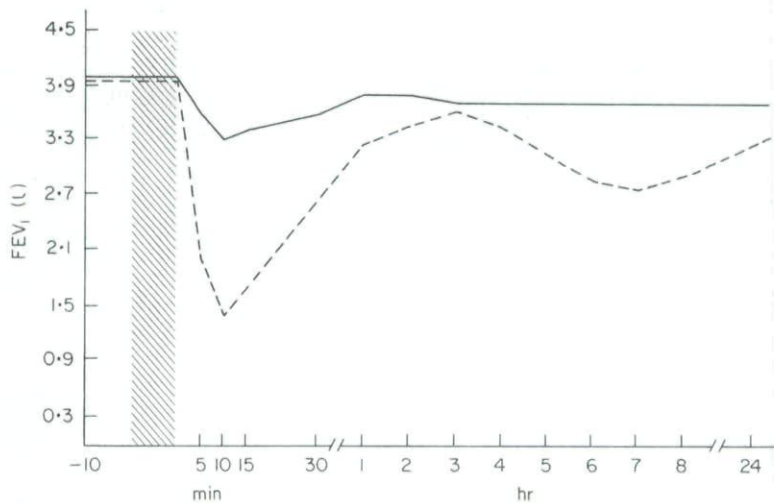


Fig. 1. Patient J.C.C., results of the provocation tests with bromelin. (---) Bromelin, (—) lactose. (■) Challenge period.

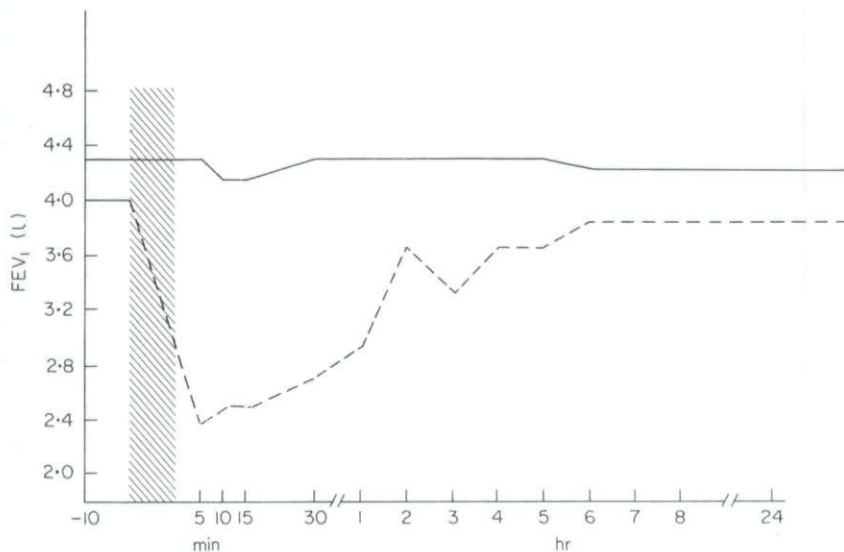


Fig. 2. Patient L.R.T., results of the provocation tests with bromelin. (---) Bromelin, (—) lactose. (■) Challenge period.

antigen, whereas case 2 is atopic, his prick test results are positive for other antigens, and sensitization required only a light exposure to a powerful antigen.

The fact that the latter patient suffered an asthmatic attack from the ingestion of pineapple shows absorption of these enzymes from the digestive tract, and suggests the probability of this pathway for sensitization, which may well have been prior to inhalation.

These findings should alert physicians to a problem that is likely to increase and will require prevention, insofar as it is possible.

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