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Occupational asthma caused by linseed oilcake

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Key words: asthma; bronchoprovocation tests; linseed; occupational diseases.

Linseed oil, extracted from the common flax seed (*Linum usitatissimum*, botanical family of *Linaceae*), has been used for centuries as an ingredient for paints, varnishes, wood preservatives, soaps, inks, and floor coverings. This vegetable oil is currently enjoying a revival as a source of renewable and biodegradable material in the production of lubricants and coatings. Furthermore, cold-pressed linseed oil is used for human consumption as a bakery additive, a bulk laxative, and a nutritional supplement because of its high content in omega-3 fatty acids. Linseed oilcake, the solid residue resulting from the extraction process, is suitable for cattle feed.

Inhalation of linseed dust is a potential cause of IgE-mediated respiratory disease in the bio-polymer industry.

The IgE-mediated anaphylactic reactions to linseed have occasionally been reported in relation to the ingestion of bulk laxatives (1, 2) and multigrain bread (3). In the early 1960s, occupational rhinitis and asthma caused by linseed had been documented through skin testing in seamen, dockers, and oil-processing plant workers in Marseilles, France (4). Herein, we describe an oleochemical plant worker who developed occupational rhinitis and asthma induced by the inhalation of linseed oilcake dust.

A 33-year-old chemist experienced work-related rhino-conjunctivitis symptoms 30 months after starting employment in the research laboratory of a plant that producing new vegetable oil-based bio-polymers. The symptoms occurred electively when the subject went to the extraction department to collect samples of ground linseed oilcake to measure its protein content. Approximately 2 years later, he developed asthma symptoms that occurred most often at the end of his work shift or after having left the workplace. The subject had never smoked and did not report any personal history of atopic disease or food allergy.

Skin prick tests were completed using increasing concentrations of a linseed extract prepared by stirring ground linseed oilcake in sterile saline solution for 1 h at room temperature. The resulting solution was passed through a 0.22-μm Millipore filter (Millipore Corp., Bedford, MA, USA). The 1 mg/ml solution of linseed elicited an immediate 5-mm skin reaction. Skin prick tests with raw and refined oils of linseed provided negative results, likewise with a battery of common inhalant allergens. The subject's serum exhibited a high level of specific IgE against linseed (> 100 IU/ml) using the ImmunoCAP method (Phadia Diagnostics, Uppsala, Sweden).

Specific inhalation challenges were performed 1 month after the subject had left his job because of his respiratory symptoms. Baseline spirometry showed a forced expiratory volume in one second (FEV_1) of 4.44 l (104% pred) and an FEV_1/forced vital capacity ratio of 74%. A control challenge with lactose powder for 30 min did not induce any significant changes in FEV_1 over the following 6 h (Fig. 1). At the end of this control day, the concentration of histamine causing a 20% fall in FEV_1 (PC_{20}) was 14 mg/ml. The analysis of induced sputum showed a total cell count of 1.1×10^6 cells/ml with 1% eosinophils. On the next day, tipping linseed 1/1000 for 25 min resulted in a dual asthmatic reaction. Twenty-four

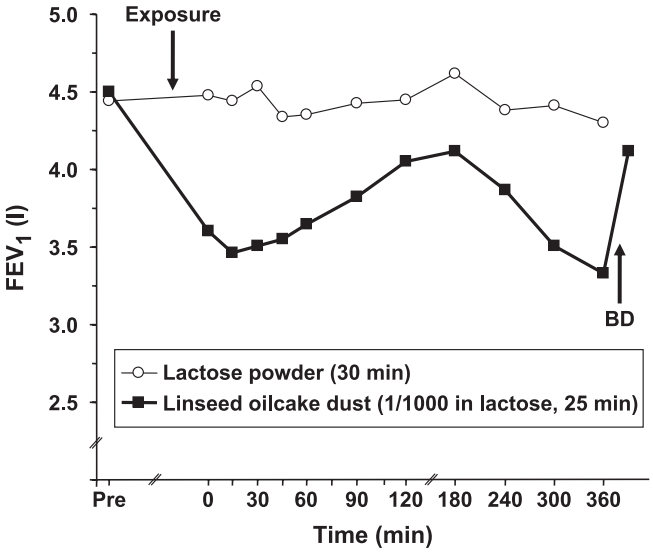

Figure 1. Results of specific inhalation challenges illustrating the changes in forced expiratory volume in 1 s (FEV_1) after exposure to lactose powder (open circles) and to linseed oilcake dust diluted 1/1000 in lactose (closed circles).

hours after the end of challenge exposure, histamine PC_{20} value was decreased significantly to 1.35 mg/ml while sputum eosinophils were increased substantially (19% of 4.76×10^6 cells/ml) as compared with the control day values.

To the best of our knowledge, this is the first case of linseed-induced occupational asthma confirmed by inhalation challenges since the original description by Prof. Charpin et al. (4). More importantly, this report should draw renewed attention to the sensitizing potential of linseed and other oleaginous seeds that are expected to be increasingly used as environmentally friendly alternatives to petroleum-derived materials. Airborne exposure to these vegetable allergens should be minimized through appropriate work hygiene measures.

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IgE-mediated anaphylaxis to proton pump inhibitors – cross-reacting study

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Key words: anaphylaxis; drug allergy; omeprazole; pantoprazole; proton pump inhibitors.

A 37-year-old woman attended our department, who reported that 3 months ago, she had taken an omeprazole capsule for peptic ulcer and after 15 min, itching of the palms, facial angioedema, generalized urticaria, bronchospasm, dizziness and collapse occurred. No other drugs had been administered during the previous 12 h. She was immediately transferred to the emergency services and received adrenaline, dimenthidene, hydrocortisone and nebulized β_2-agonists. In the past, she had taken omeprazole many times. She had no history of atopy.

PPIs are a rare cause of anaphylaxis. Cross-reactivity at the whole group should not be assumed.

We conducted skin prick test (SPT) with commercial common inhalant, food allergens and other imidazole derivatives (ketokonazole, metronidazole), which was negative. SPT with lansoprazole, pantoprazole, rabeprazole and esomeprazole was negative too. The skin prick and intradermal tests to omeprazole were positive.

Serum sample, tested in Phadia Laboratories (CAP – FEIA), was negative for specific IgE to omeprazole. Challenges with lansoprazole, panteprazole and capsule shell showed no reactions.

Two months before attending our department, a 58-year-old male had suffered generalized urticaria vomiting and diarrhea 1 h after taking an omeprazole capsule.

Fifteen days later, he received an i.v. injection of pantoprazole before an operation. Because of previous reaction to omeprazole, doctors preferred pantoprazole as a safer choice. Five minutes after injection, he had generalized itching, shock and loss of consciousness.

Our study showed that SPT and ID tests were positive to omeprazole and pantoprazole. Skin prick test to esomeprazole, lansoprazole and rabeprazole was negative. A challenge test with esomeprazole was negative. The patient refused challenges to other PPIs.

Skin prick test to omeprazole, pantoprazole, esomeprazole, lansoprazole, rabeprazole and ID tests to omeprazole and pantoprazole were negative in five normal controls (Table 1).

Our patients had experienced anaphylactic reactions, the first one to omeprazole and the second one to omeprazole and pantoprazole, as suggested by the history and positive skin tests. Other causes of anaphylaxis, such as food, drugs, insect sting or capsule shell were excluded.

In our study, skin tests with proton pump inhibitors (PPIs) proved to be the only accurate and simple method of identification of the incriminated agent and quite specific to solve cross-reactivity problems among drugs of this group. This conclusion is in accordance to the vast majority of the studies (1, 2).

Serum specific IgE tao omeprazole could not be measured by CAP method in our patients and this result is in line with most studies (3–5). There is only a case report with positive basophil activation test (F.A.S.T) to omeprazole in literature (6).

The causative factor for anaphylactic reactions to PPI in our patients was the original molecule (omeprazole and pantoprazole) and not any metabolite as revealed by positive skin test and oral challenge.

Oral provocation tests with PPIs in patients with negative skin tests proved to be a safe and effective procedure for identifying an alternative safe drug of this group (1).

A very impressive finding was that the second patient sensitive to omeprazole tolerated esomeprasole, an *S*-enantiomer of omeprazole.

The most reports of anaphylactic reactions demonstrate the presence of cross-reactivity among PPIs to extend to the whole group (2, 5) but in our patients, the sensitization was proved to be restricted to one and two compounds respectively according to skin and oral challenge tests (1).

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