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Occupational rhinitis to sodium alendronate

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Key words: alendronate; allergy; bisphosphonate; occupational rhinitis; sensitization.

Sodium alendronate (SA) is a low-molecular-weight (LMW) compound inhibiting bone resorption, used to treat osteoporosis, recognized as an irritant of the respiratory system and skin.

A few cases of skin reaction after oral intake of bisphosphonate have already been reported (1, 2). To our knowledge, no report exists on occupational respiratory allergy caused by this compound.

A 40-year-old woman was referred to our department for suspected work-related rhinitis and asthma. Since 1995 she had been employed in a pharmaceutical company, assigned to the tablets packaging department of SA (about 1 week each month) and other drugs, and particularly during the 3 months before our observation she was employed exclusively on the SA line. The product line was enclosed, provided with local exhaust fans, and the subject wore a mask without a particle filter. One month after being moved exclusively to the SA line, she started to complain of nasal itching,

rhinorrhoea and dry cough. Symptoms appeared every Monday, 1 h after starting her work, improved during weekends and resolved during holidays. Symptoms were more severe during day shifts than during night shifts, when only less number of lines was involved in the production. No similar symptoms were reported by other employees.

The patient came to our observation 1 month after the symptoms' onset; she had worked until the day before our consultation.

The clinical history reported wheals after strawberry ingestion, palmo-plantar erythema after intake of an unspecified antibiotic, eczema after use of latex gloves and sneezing upon exposure to cats. She had never taken SA.

Lung function tests were normal, skin prick tests (SPTs) were positive to cat dander and grass pollens, serum IgE levels were 36.8 kU/l and peripheral eosinophilia was 4.3%.

Both SPTs and patch tests with SA in saline (1 : 100 and 1 : 10 w/v) were positive, and showed negative results when performed on 10 nonexposed subjects.

A specific Inhalation Challenge (SIC) was performed, out of grass pollens period, with occupational method (3). After a control day, exposure for 60 min to SA 10 mg dissolved in lactose provoked a significant increase in nasal symptoms' score and a significant decrease in peak nasal inspiratory flow (PNIF) at 15, 30 and 240 min, but no change in forced expiratory volume in 1 s (FEV₁). After SA exposure, provocative dose of methacholine producing a 20% fall in FEV₁ (PD₂₀ FEV₁) decreased from 1636 µg before challenge to 704 µg and induced sputum (IS) eosinophils increased from 1.2% to 7.9% (4).

The SIC repeated after premedication with oral levocetirizine induced no significant change in PNIF. SIC was also performed in a healthy control with no significant change.

A diagnosis of allergic occupational rhinitis (OR) caused by SA was made (5). During follow-up visit, the patient had ceased exposure to SA and was completely free of symptoms.

Among LMW-chemicals, several drugs are well-known to induce work-related respiratory allergy (6). To our

knowledge, this is the first case, described in the literature, of OR caused by SA. The patient's history, SPTs, patch tests and the SIC results fulfilled the criteria for the diagnosis of OR caused by SA (5). The presence of a latency period, the dual nasal response to SIC, the absence of symptoms in other exposed workers suggest an allergic mechanism.

Interestingly, sensitization occurred despite the enclosure of the production process and the use of a personal protective device (mask). It may be suggested that during the loading phase of tablets, some powder disperses into the environment and the mask proved inadequate. The observed decrease in PD₂₀ FEV₁ and increase in IS eosinophils may be related to lower airways' inflammation induced by the nasal response and/or may have represented an early, preclinical marker of occupational asthma (OA). The negative response to SIC after levocetirizine suggests that mast cells may play a role in the response.

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Asthmatic reaction induced by Etoricoxib in a patient with aspirin-sensitive asthma

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Key words: aspirin; asthma; drug allergy; Etoricoxib; oral challenge.

The use of selective cyclooxygenase-2 (COX-2) inhibitors as an alternative to other nonsteroidal anti-inflammatory drugs (NSAID) is suggested for patients with aspirin-induced asthma. The safety of Rofecoxib (1, 2) and of Celecoxib (3) was demonstrated in these patients with double-blind, placebo-controlled oral challenges.

We present the case of a 64-year-old woman with aspirin-sensitive asthma and a history of severe anaphylactic reactions to different NSAID, who developed an asthmatic reaction after a single-blind, placebo-controlled oral challenge with Etoricoxib. She reported that 30 years ago, she had developed bronchial asthma with sensitization to house dust mites. Initially, there were some moderate asthmatic reactions to aspirin, one severe anaphylactic reaction to two tablets of Copyrkal® (400-mg paracetamol and

50-mg caffeine) and one nearly life-threatening anaphylactic reaction after an i.v. injection of metamizole, a pyrazolone drug. Ten years ago, she had surgery on nasal polyps and, to date, she has noticed a moderate relapse of nasal polyposis. In the past few years, the asthma has been difficult to treat and for nearly the whole of the year prior to presentation an oral prednisolone therapy between 20 and 50 mg a day was necessary. At the time of presentation her medication was a high-dose inhalative and topical nasal corticosteroid, a long-acting β -agonist, oral low-dose theophylline and an H1-antihistamine. At least three times a week she needed a short-acting β -agonist at night. After the last severe exacerbation of her asthma, the oral prednisolone therapy was now stopped 2 weeks before admission. Blood tests and leukocyte differential count were within normal limits. Total serum IgE was 227 kU/l, specific IgE to *Dermatophagoides pteroniss* was 0.63 kU/l (RAST class 1). The physical examination and lung function were normal. Before starting an adaptive desensitization with aspirin, a single-blind, placebo-controlled oral challenge with Etoricoxib as an alternative analgetic drug was conducted. At 1-h intervals, first two dosages of placebo and then 30 and 60 mg of Etoricoxib were administered. Thirty minutes after the 60 mg Etoric-

oxib dosage she complained about moderate dyspnoea. The clinical examination revealed severe rhinorrhoea and a shortness of breath with wheezing. The lung function showed a fall in forced expiratory volume in 1 s (FEV₁) of 24% from baseline, and an increase in specific resistance of 120% to 3.5 kPa $\times$ s (Fig. 1). After the administration of a short-acting β -agonist and 50 mg prednisolone i.v. the symptoms resolved. A single-blind, placebo-controlled oral challenge with paracetamol was tolerated well up to a dosage of 500 mg. Then, an adaptive desensitization with aspirin was initiated. The patient reacted to 20-mg aspirin with moderate rhinorrhoea and a fall in FEV₁ of 22% from baseline. With the administration of a short-acting β -agonist and repeating the 20 mg dosage twice, the adaptive desensitization could be finished without any further adverse effects up to 500 mg/day aspirin.

Etoricoxib is a second-generation COX-2 inhibitor with the highest *in vitro* selectivity for COX-2. In a double-blind, placebo-controlled trial comparing Etoricoxib (120 mg) and Celecoxib (200 mg) in patients with NSAID-induced urticaria or angioedema, the reaction rate was 11% for Celecoxib and 7% for Etoricoxib, but without any asthmatic reaction (4). In 31 patients with intolerance to NSAIDs, manifested as cutaneous, respiratory or

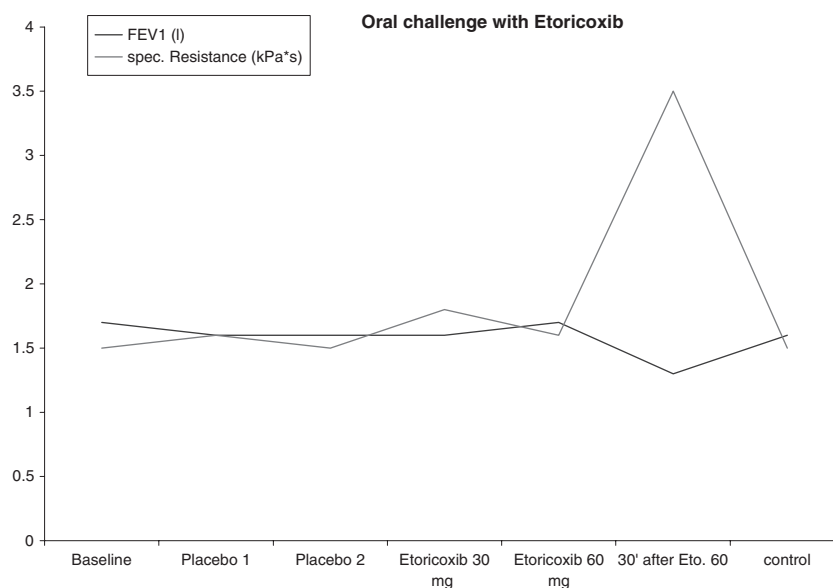


Figure 1. Oral challenge with Etoricoxib.