

Occupational asthma and rhinitis induced by a cephalosporin intermediate product: description of a case

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Key words: 7-TACA; cephalosporin; occupational asthma; occupational rhinitis; specific inhalation challenge.

7-Amino-3-thiomethyl-3-cephalosporanic acid (7-TACA) is an intermediate product in cephalosporins' synthesis. Few cases of occupational asthma (OA) due to cephalosporins (1) and to their intermediate product 7-TACA (2) have been reported, but no report exists on OA due to 7-TACA nor on occupational rhinitis (OR) induced by cephalosporins or intermediate products.

A 44-year-old man was referred to our department for evaluation of work-related respiratory symptoms. Since July 2007 he had been employed in a pharmaceutical company, assigned to cephalosporins' product line. The product line was enclosed except for loading phases, during which the raw materials and intermediate products (7-TACA) were poured into reactors. Eight months after starting that job, he began to complain of sneezing, and 1 month later of dry cough and shortness of breath. In July 2008 he experienced severe dyspnoea requiring hospitalization after a loading operation. Thereafter he was moved to the corticosteroid product line and became completely asymptomatic.

He came to our observation 4 months after the last exposure to 7-TACA. Personal history of allergy was negative.

No similar symptoms were reported by other employees.

The patient underwent the common diagnostic pathway for OA (3) and OR (4). Lung function tests were normal, skin prick tests (SPTs) to common allergens were positive for house dust mites. Serum IgE levels were 98.9 kU/l and peripheral eosinophilia 1.1%.

SPT with 7-TACA was not performed because the compound was not soluble in saline. A Specific Inhalation Challenge (SIC) with occupational method was carried out (5). Before and after SIC nasal secretions (NS) and induced sputum (IS) were collected, methacholine (MCH) challenge test was performed and serum tryptase and eosinophils in peripheral blood were detected.

After a control day in which the patient was exposed to lactose, exposure to 0.5% 7-TACA mixed with 99.5 mg of lactose in a 7.46 m³ inhalation challenge room (6), elicited dyspnoea after 5 min of exposure and was interrupted. Spirometry showed a 22% FEV₁ fall which decreased up to 32% at 15 min after the end of exposure. Salbutamol (200 µg) was administered followed by a FEV₁ increase up to -4%. An increase in nasal symptoms' score and a decrease in peak nasal inspiratory flow (from 140–0 l/min) at 15 min were observed. Nasal eosinophils increased from 2.9% (1.85×10^4 /ml) before challenge to 24.8% (19.34×10^4 /ml) 4 h

after challenge (Fig. 1). No change in IS eosinophils was observed before and after SIC. MCH challenge test was negative before and after SIC. No significant variation in serum tryptase and peripheral eosinophilia was found after SIC. To assess the specificity of the response SIC was performed in a 37-year-old atopic healthy control with the same method for 30 min of exposure to 7-TACA, resulting negative. A diagnosis of OR and OA caused by 7-TACA was made. To the best of our knowledge this is the first case of OR and OA due to 7-TACA and the first reported case of OR due to a cephalosporins intermediate product. The immediate response to SIC after few minutes of exposure may suggest an aspecific, irritative mechanism. Nevertheless, the low level of exposure during the SIC, the presence of a latency period (exposure/symptoms' onset), the absence of similar symptoms in other exposed subjects, the delayed increase in nasal eosinophils after SIC and the negative SIC in the healthy control confirm the specificity of the response, suggesting an immunologic mechanism. Interestingly, the exposure to the causative agent elicited an increase in nasal but not in sputum eosinophils. We may suppose that the very short time of exposure to 7-TACA (5 min) during the SIC has been insufficient to induce a recruitment of eosinophils in the lower airways.

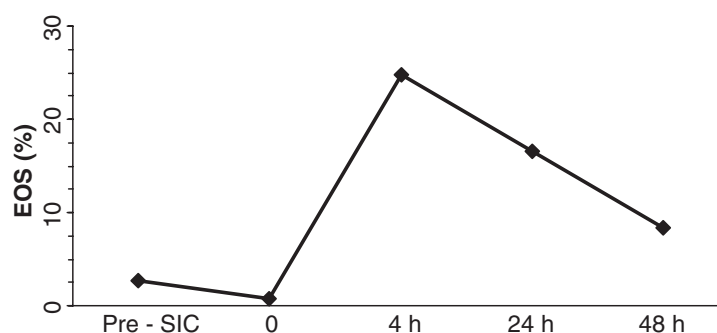


Figure 1. Nasal eosinophil response to Specific Inhalation Challenge (SIC).

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References

1. Sastre J, Quirce S, Novalbos A, Lluch-Bernal M, Bombín C, Umpierrez A. Occupational asthma induced by cephalosporins. *Eur Respir J* 1999;**13**: 1189–1191.
2. Park HS, Kim KU, Lee YM, Choi JH, Lee JH, Park SW et al. Occupational asthma and IgE sensitization to 7-aminocephalosporanic acid. *J Allergy Clin Immunol* 2004;**113**:785–787.
3. Malo JL, Chan-Yeung M. Occupational asthma. *J Allergy Clin Immunol* 2001;**108**:317–328.
4. Moscato G, Vandenplas O, Gerth Van Wijk R, Malo JL, Quirce S, Walusiak J, et al. Occupational rhinitis. *Allergy* 2008;**63**:969–980.
5. Vandenplas O, Cartier A, Malo JL. Occupational challenge test. In: Bernstein IL, Chan-Yeung M, Malo JL, Bernstein DI, editors. *Asthma in the workplace*. New York: Taylor & Francis, 2006:227–252.
6. Moscato G, Galdi E, Scibilia J, Dellabianca A, Omodeo P, Vittadini G et al. Occupational asthma, rhinitis and urticaria due to piperacillin sodium in a pharmaceutical worker. *Eur Respir J* 1995;**8**:467–469.