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ORIGINAL ARTICLE

Occupational asthma caused by triglycidyl isocyanurate

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Abstract
Background Several cases of allergic contact dermatitis, two cases of occupational asthma from over one decade ago and one case of hypersensitivity pneumonitis have been documented in painters who use polyester powder paint containing triglycidyl isocyanurate (TGIC).
Methods We report a 28-year-old female who, 4 months after beginning work in a powder-coating factory, developed asthma-like symptoms. In her workplace, aluminium frames were treated with an electrostatic powder paint containing 2.5–10% TGIC.
Results Serial peak-flow measurements performed during both working and non-working periods demonstrated peak-flow variability of up to 46% on work days. Bronchial methacholine test results also varied between times at work and away from work. PC_{20} methacholine was 0.32 mg/ml and fraction of exhaled nitric oxide (FENO) was 18 ppb. A controlled exposure challenge was performed with a placebo yielding no changes in FEV_1 over a 24-hour period. On visit 2, the patient was placed in the chamber and exposed to TGIC (4% in lactose) at a mean concentration of 3.61 mg/m^3 for a total of 15 min. A 20% fall in FEV_1 from baseline was elicited at 10 min, together with cough and wheezing. No late response was demonstrated. Twenty-four hours after the challenge, neither methacholine PC_{20} nor FENO levels varied from baseline values. No IgE was detected by ELISA testing and no IgE-binding bands were found by immunoblot analysis of patient and control serum.
Conclusions The aforementioned results demonstrate that TGIC inhalation induced immunologic occupational asthma, although no IgE mechanism was evidenced.

Keywords Occupational asthma · Triglycidyl isocyanurate · Polyester powder paints · Epoxy compound

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Introduction

Polyester powder paints are used extensively in metal painting. Exposure to these substances may give rise to hypersensitivity pneumonitis (Piirilä et al. 1997a) and late asthmatic reactions accompanied by fever and leukocytosis (Cartier et al. 1994), which are thought to be caused by the acid anhydrides contained in the paint (Piirilä et al. 1997a; Cartier et al. 1994). Triglycidyl isocyanurate (TGIC) is an epoxy compound often used as a hardener in these paints. TGIC ($C_{12}H_{15}N_3O_6$), a synthetic white powder or granule with no discernible odor at room temperature, is used mainly as a three-dimensional cross-linking or curing agent in polyester powder coatings (paints). TGIC does not occur naturally, but rather is manufactured by reacting cyanuric acid with excess epichlorohydrin (Willcocks et al. 1998). Triglycidyl 2 isocyanurate is also used in solder "mask" inks in the printed circuit board industry. The two-part inks contain ~60% TGIC in the hardener component. Much of

the TGIC in powder coatings and solder inks is immobilized through cross-linking in an insoluble matrix. Worldwide production of TGIC is ~7,000–8,000 tons per year (Willcocks et al. 1998). Powder coatings usually contain 4–10% TGIC and are sprayed onto metal objects by an electrostatic process. The coated metal objects are then treated in an oven at a temperature of about 200°C. This heating causes the powder coatings to melt, flow, and chemically cross-link.

Occupational exposure to TGIC occurs during the manufacture and use of products containing the chemical. Little information is available on the effects of TGIC in humans. Several cases of allergic contact dermatitis (Wigger-Alberti et al. 1997), two cases of occupational asthma from more than one decade ago (Piirilä et al. 1997b; Meuleman et al. 1999), and one case of hypersensitivity pneumonitis (Quirce et al. 2004) have been documented in painters using polyester powder paint containing TGIC.

Case report

We report a 28-year-old female former smoker who stopped smoking 5 years ago who, 4 months after beginning work in a powder-coating factory, developed recurrent episodes of cough, dyspnea, shortness of breath, and wheezing in the evening and at night. She was treated with salbutamol as needed. In her workplace, aluminium frames were treated with an electrostatic powder paint whose product label and material safety data sheets indicated that the product contained 2.5–10% TGIC. The polyester powder paint was sprayed through injectors onto metallic boards in an open tunnel and then heated and dried in an oven. The patient did not use any protective clothing, gloves, or mask at work. Serial peak-flow measurements performed during both working and non-working periods demonstrated peak-flow variability of up to 46% on work days and up to 10% on non-work days. Bronchial methacholine test results also varied between periods of work (PC20 0.4 mg/ml) and periods away from work (methacholine PC20 4 mg/ml).

The patient was evaluated while on sick leave and 4 months after leaving her position. Physical examination, blood tests, and spirometry results were normal. Skin prick test with common inhalants were negative. On the first day, PC_{20} methacholine was 0.32 mg/ml and fraction of exhaled nitric oxide (FENO) was 18 ppb, performed as previously described (Fernández-Nieto et al. 2009). After obtaining written informed consent, an exposure challenge was performed with a placebo (lactose as sham exposure) by placing the patient in a 7 m^3 chamber for 30 min; this challenge yielded no changes in FEV_1 over a 24-h period, with values measured hourly by means of a computerized flow meter (Amos, Jaeger, Germany) except when the patient was sleeping. On visit 2, the patient was placed in the chamber once again and exposed to TGIC (4% in lactose, TGIC is a fine powder at room temperature, Naber SA, Valencia, Spain) at a mean concentration of 3.61 mg/m^3 of total dust (DustTrack, model 8520, TSI instruments, Shoreview, USA) for a total of 15 min. The mixture was passed from one tray to another to produce a cloud of dust. A fall in FEV_1 of 20% from baseline was elicited at 10 min, together with cough and wheezing. No late response was demonstrated. Twenty-four hours after the challenge, neither methacholine PC_{20} nor FENO levels varied from baseline values.

Specific IgE antibodies to TGIC were determined by direct enzyme-linked immunosorbent assay (ELISA) and Western blot analysis. TGIC was conjugated with human serum albumin (HSA) as previously described (Quirce et al. 2004) and dialyzed against ammonium bicarbonate 0.02 M for 48 h. Immulon 4 microplates were coated with TGIC-HSA or HSA at a concentration of 10 μg/ml (Quirce et al. 2004). No IgE was detected by ELISA testing and no IgE-binding bands were found by immunoblot analysis of patient and control serum.

Discussion

We demonstrate a specific immediate asthmatic reaction to TGIC during a controlled bronchial challenge test in a worker exposed to this product. Previously, a PEF-flow monitoring and a methacholine test follow-up showed a typical pattern of occupational asthma during the period of work. However, these tools only demonstrate association between pulmonary function tests and working and non-working periods but not the etiologic agent, since immunologic study was negative. Methacholine PC20 nor FENO values varied after immediate asthmatic reaction which is seen in cases of isolated immediate asthmatic reactions (Sastre et al. 2003).

The aforementioned results demonstrate that TGIC inhalation induced immunologic occupational asthma, although no IgE mechanism was evidenced. To our knowledge, this is the third report of occupational asthma due to TGIC.

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Conflict of interest None.

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