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CASE REPORT

Occupational asthma caused by an epoxy amine hardener

O. Vandenplas[1,2], C. Rifflart[1], G. Evrard[1], J. Thimpont[2], M. Seed[3] and R. Agius[3]

[1]Department of Chest Medicine, Centre Hospitalier Universitaire UCL Namur, Université Catholique de Louvain, Yvoir B-5530, Belgium, [2]Medical Department, Agence fédérale des risques professionnels (Fedris), Brussels B-1210, Belgium, [3]Centre for Occupational and Environmental Health, School of Health Sciences, The University of Manchester, Manchester M13 9PL, UK.

Correspondence to: O. Vandenplas, Department of Chest Medicine, Centre Hospitalier Universitaire UCL Namur, Université Catholique de Louvain, B-5530 Yvoir, Belgium. Tel: +32 81 42 33 63; fax: +32 81 42 33 52; e-mail: olivier.vandenplas@uclouvain.be

Abstract We describe a 43-year-old epoxy floor layer who developed work-related asthma while exposed to an epoxy hardener based on isophorone diamine (IPDA). Challenge exposures to the curing of the epoxy resin system and subsequently to the polyfunctional amine hardener containing IPDA both elicited delayed asthmatic reactions. This report further indicates that exposure to epoxy hardeners containing polyfunctional amines should be considered as a potential cause of occupational asthma. Appropriate work hygiene measures should be implemented to minimize airborne exposure to these volatile compounds.

Key words Amines; asthma; bronchoprovocation tests; occupational diseases.

Introduction

Epoxy resins have a broad range of industrial applications as protective surface coatings, adhesives, insulation material for electrical components and manufacture of fibre-reinforced composites [1]. The basic components of epoxy resin systems include epoxy resins, mainly based on monomers or polymers of diglycidyl ether of bisphenol A and hardeners, mainly aliphatic and cycloaliphatic polyfunctional amines (Figure 1). These epoxy resin components are among the most common causes of occupational allergic contact dermatitis [1]. Although sensitizer-induced occupational asthma (OA) caused by other resin hardeners such as isocyanates, acid anhydrides and acrylates has been well documented [2], few cases of OA due to polyamine hardeners [3,4] have so far been described. We describe a case of OA due to a polyfunctional amine hardener in an epoxy floor layer in whom the diagnosis was documented through specific inhalation challenges (SIC).

Case report

A 43-year-old non-smoking man developed work-related asthma symptoms ~3 years after having started his employment as a concrete epoxy floor coater. He experienced wheezing and chest tightness that occurred 3–5 h after having been exposed to the curing of an epoxy coating applied on the floor of industrial and public buildings. The asthma symptoms persisted in the evening and frequently induced nocturnal awakenings. They usually recurred for 2–4 days after epoxy floor coating. He took a short-acting inhaled bronchodilator (salbutamol) up to 10 times a day when exposed to the epoxy resin curing. He reported neither rhinitis nor cutaneous symptoms related to epoxy resin exposure. According to the safety data sheets provided by the manufacturer, the epoxy component of the resin was based on diglycidyl ether of bisphenol A (Chemical Abstracts Service [CAS] no. 25068-38-6) and the hardener contained the cycloaliphatic polyamine isophorone diamine (IPDA or 3-aminomethyl-3,5,5-trimethylcyclohexamine, CAS no. 2855-13-2).

The patient was evaluated ~4 years after the onset of work-related asthma symptoms. Skin-prick tests with a battery of common allergens elicited a positive response to the house dust mite. Skin-prick test with the pure hardener provided negative results. The subject gave informed consent for performing SIC with the suspected epoxy resin, which were completed 3 days after removal from any workplace exposures to epoxy resin [5]. Baseline spirometry showed a forced expiratory volume in 1 s (FEV_1) of 3.39 l (105% predicted) and a forced vital capacity of 4.29 l (111% predicted). As a control challenge, the subject was exposed to

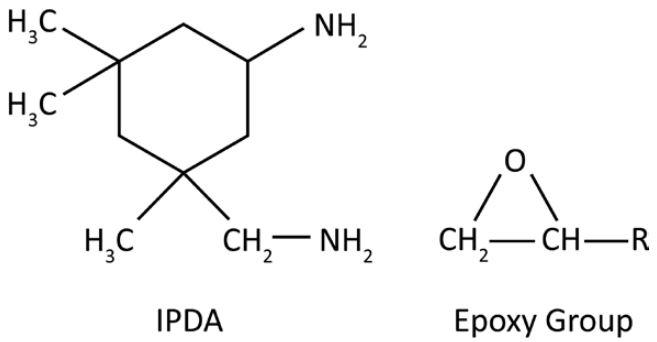

Figure 1. Chemical structure of isophorone diamine (3-aminomethyl-3,5,5-trimethylcyclohexamine). Amine groups of the hardener react with the epoxy groups of bisphenol diglycidyl ethers to form polymeric resins.

a nebulized paint diluent nebulized in the challenge room for 30 min without inducing significant changes in FEV_1 over the following 6 h (Figure 2). At the end of this control day, the concentration of histamine causing a 20% fall in FEV_1 (PC_{20}) measured using the tidal breathing method was 7.6 mg/ml, indicative of slight nonspecific bronchial hyperresponsiveness (normal value > 16 mg/ml) [6]. Sputum induction failed to provide a sample suitable for cell analysis.

On the next day, SIC was carried out simulating his work activity by mixing the epoxy resin and the hardener in a 3:1 ratio without the epoxy diluent until complete curing (Figure 2). During the curing process, the temperature of the mixture rose to 120°C. The patient was exposed for gradually increasing periods of time up to 2 h without recording significant changes in FEV_1 [5]. Starting 60 min after the end of challenge exposure, the FEV_1 showed a progressive decline reaching −38% from pre-SIC value recorded 4-h post-exposure, and the patient was then administered inhaled salbutamol. Twenty-four hours after the end of challenge exposure, the histamine PC_{20} was decreased to 2.9 mg/ml. The concentration of exhaled nitric oxide (FeNO) was increased to 139 ppb as compared to 79 ppb at the pre-exposure assessment.

One month later, the histamine PC_{20} value was measured at 4.0 mg/ml. In the next morning, the subject was exposed to the liquid epoxy hardener (50 ml) heated to 40°C (Figure 2). A cumulative exposure of 60 min resulted in a delayed asthmatic reaction with a maximal fall in FEV_1 of 38% from pre-SIC value recorded 5 h after the end of exposure. On the following morning, FEV_1 was still 22% lower than the pre-challenge value and the histamine PC_{20} was not re-assessed. FeNO increased from 131 ppb in the morning before challenge exposure to 177 ppb 24 h after the end of exposure.

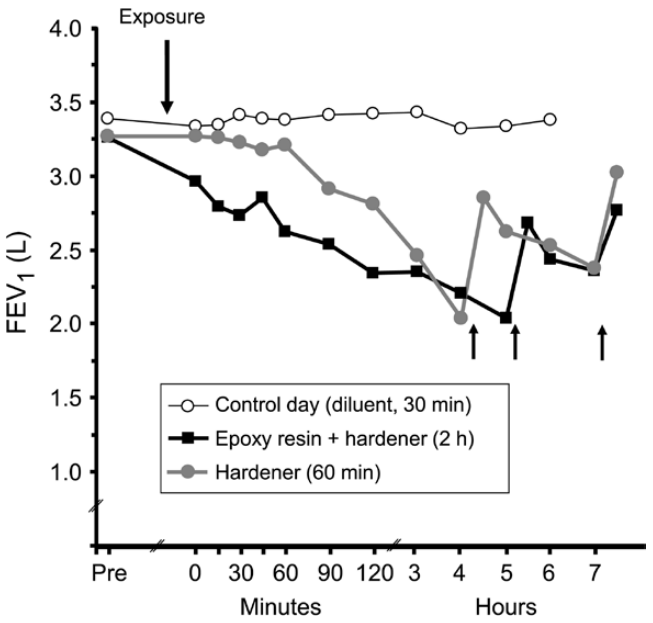

Figure 2. Results of inhalation challenges illustrating the changes in FEV_1 after exposure to a control agent (nebulized paint diluent) for 30 min (open circles), the epoxy resin mixed with the hardener for 2 h (black closed squares) and the hardener alone heated to 40°C for 60 min (grey closed circles). Vertical arrows indicate administration of inhaled salbutamol (400 µg).

Discussion

Separate SICs to the curing of the whole epoxy resin system and to the heated polyfunctional amine hardener containing IPDA elicited delayed asthmatic reactions as well as an increase in the post-SIC level of non-specific bronchial hyperresponsiveness to histamine and FeNO, a marker of airway eosinophil inflammation [7]. These features provided evidence supporting a diagnosis of sensitizer-induced OA caused by the polyfunctional amine hardener IPDA.

Although a number of amines used in a wide variety of industrial applications have been documented as causing OA [8], we were able to identify only two detailed case reports of OA caused by epoxy hardeners containing aliphatic amines (i.e. trimethyl 1,6-hexanediamine [CAS no. 25620-58-0] and tetraethylene pentamine [CAS no. 112-57-2]), the cycloaliphatic IPDA (CAS no. 2855-13-2) and an aromatic amine (i.e. 4-4′-diaminodiphenyl methane [CAS no. 101-77-9]) [3,4].

The pathophysiologic mechanisms involved in the induction of OA by low-molecular-weight occupational agents remain largely unknown [9]. These agents have to combine with an amino acid side chain of a native protein molecule present in the respiratory tract to initiate a specific immune response. A computer-based quantitative structure-activity relationship model aimed at quantifying the asthmagenic potential of low-molecular weight agents found that an OA hazard index of 0.39 is able to distinguish asthmagenic compounds from non-asthmagenic compounds with a sensitivity of 90% and a specificity of 96% (http://www.coeh.man.ac.uk/asthma/login.php) [10]. IPDA has an asthma hazard index of 0.49, while the diglycidyl ether of bisphenol A has a low index of 0.14.

This report provides further evidence that exposure to volatile polyamine epoxy hardeners is associated with

a potential asthma hazard. Awareness of this possibility may be important in view of the widespread use of epoxy resins [1].

Key points

- This case study provides further evidence that inhalation exposure to polyfunctional amine hardeners can induce occupational asthma through a presumably sensitizing mechanism.
- Awareness of the asthmagenic potential of amine hardeners may be important in view of the widespread use of epoxy resins.
- Work hygiene measures aimed at reducing inhalation exposure to amine compounds should be implemented.

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Conflict of interest

There is no conflict to declare in relation to this article.

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