

Occupational allergic airborne contact dermatitis caused by pethoxamid – a new herbicide

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Allergic contact dermatitis caused by herbicides is rare. We present a case of occupational allergic contact dermatitis caused by pethoxamid, a herbicide registered in Europe for use on corn, winter rape, soybeans, peas, and beans.

Case Report

A 49-year-old male, non-atopic industrial chemical worker with no past history of dermatitis presented with facial dermatitis after manufacturing pethoxamid [2-chloro-*N*-(2-ethoxyethyl)-*N*-(2-methyl-1-phenylprop-1-enyl)acetamide; CAS no. 106700-29-2; Cheminova, Lemvig, Denmark]. The patient had been working in the factory manufacturing pethoxamid for 3.5 years, without experiencing dermatitis. By accident, some pethoxamid came into direct contact with the dorsum of his right hand, and on the next day a weeping dermatitis appeared. His general practitioner prescribed a short course of oral prednisolone, and the dermatitis healed. After that, he changed his work site in the factory to a control room. However, the next five times he passed through the area where pethoxamid was produced, acute



Fig. 1. Patch test reactions to the pethoxamid dilution series on D3 (from the top: 1%, 0.5%, 0.3%, 0.05%, 0.03% and 0.01% in ethanol).

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dermatitis of the periorbital area and the ears developed. He was subsequently transferred to another work site in the factory, and the dermatitis has not recurred.

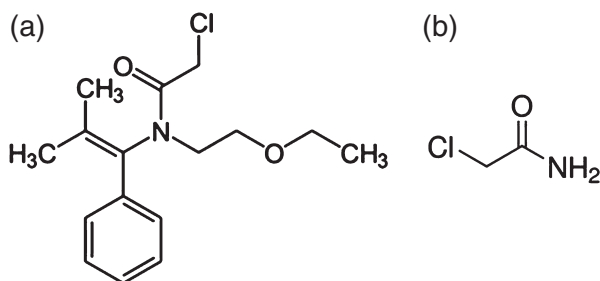


Fig. 2. Structural formulas of pethoxamid (a) [2-chloro-N-(2-ethoxyethyl)-N-(2-methyl-1-phenyl-1-propen-1-yl)acetamide] and chloroacetamide (b).

Patch testing was performed with the European baseline series [TRUE Test[®] panel 1–3 (SmartPractice Mekos, Hillerød, Denmark)] supplemented with the remaining baseline allergens in Finn Chambers[®] on Scanpor[®] tape (SmartPractice, Phoenix, AZ, USA). Patch testing was also performed with pethoxamid (Cheminova) 1%, 0.5%, 0.3%, 0.05%, 0.03% and 0.01% in ethanol and chloroacetamide (0.2% pet.; Chemotechnique Diagnostics, Vellinge, Sweden), with the Finn Chamber[®] technique. The exposure time was 2 days, and readings were performed on day (D)3 and D7. Patch tests showed positive reactions to pethoxamid 0.03–1% (+++/++) and 0.01% (+/+) (Fig. 1), but no positive reaction to chloroacetamide. To rule out irritancy, 10 consecutive control subjects were patch tested with pethoxamid 0.01–0.1% in ethanol, and showed no positive reactions.

Pethoxamid levels were monitored at the workplace. Air collection and analyses were based on National Institute for Occupational Safety and Health methods for analysing organophosphorus pesticides (1). The sampling periods varied from 2 to 3 h. Samples were analysed by gas chromatography (Agilent[®] 6890 N GC-FID Agilent Technologies, Inc. Wilmington, Delaware, USA, pr. no. G1530N and pr. no. 19091Z-433). Toluene (Merck[®] 2900 Hellerup, Denmark, pr. no. 1.08389.2500) and acetone (Sigma-Aldrich[®] Sigma-Aldrich Denmark A/S, Copenhagen, Denmark, pr. no. 32201-2.5 L) were used as solvents. The detection level for pethoxamid was

0.00004 mg/m³. The occupational exposure limit was set to 2 mg/m³, by analogy with equivalent substances. Area and breathing zone measurements of pethoxamid were between 0.003 and 0.0003 mg/m³. Small amounts of toluene, ethyl chloride and isobutyrophenone were also detected, in total not exceeding 1% of the Danish occupational exposure limits.

Discussion

This is, to our knowledge, the first case report of occupational allergic contact dermatitis caused by pethoxamid, which has been on the European market since 2006. The concentration in air samples seems to be below threshold values from the patch test results, but this does not exclude the possibility of airborne dust particles. Pethoxamid is related to chloroacetamide (CAS no. 79-07-2; trade name COLIPA no. P27; chemical synonyms 2-chloroacetamide, acetamide, 2-chloro, α -chloroacetamide, 2-chloracetamide, 2-chloroacethanamide, and 2-chloroethanamide), a compound used as a herbicide and a known sensitizer showing structural similarities with pethoxamid, but they did not cross-react in this case (Fig. 2). Like pethoxamid, chloroacetamide is used as a herbicide, but it is also used as a cosmetic and paint preservative (2, 3). Pethoxamid is classified as a sensitizing agent, as 19 of 20 animals (95%) showed signs of allergic skin reactions in the guinea-pig maximization test (4). Pethoxamid is found in Successor[®], which is a straight formulation with pethoxamid as the only active ingredient, and in Successor-I[®], which is a mixture with the active ingredient terbutylazine (CAS no. 5915-41-3). The company has plans to develop and register new pethoxamid-based products for use in countries and on crops globally (5). Because of the strong sensitizing properties of pethoxamid, we should look for further cases of contact dermatitis in agricultural workers worldwide.

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