

Photoallergic dermatitis induced by diltiazem

Contact Dermatitis 2007; 56: 118–119

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Key words: diltiazem; patch test; photoallergy; photodistributed.

Diltiazem is used as an antihypertensive and vasodilator drug. It can produce a variety of adverse effects, some of which are dose-dependent. However, cutaneous manifestations account for up to 48% of the adverse effects (1) and are not dose-related.

We report a cutaneous photodistributed reaction associated with diltiazem in which photopatch test was useful for setting the definitive diagnosis.

Case Report

An 81-year-old woman in treatment with glicazide, clopidogrel, nitroglycerine, and diltiazem, consulted for an itchy, scaly, and photodistributed erythema. The patient had started treatment with diltiazem 6 months before the development of the erythema. It was well delimited on the face and V-neck area sparing the submentonian and retroauricular regions. It worsened with exposure to sun. The patient also had itchy lesions on the forearms and dorsum of both hands, with a lichenoid appearance.

The histopathologic examination of a skin sample from the patient's forearm showed a subacute spongiotic dermatitis with a perivascular inflammatory infiltrate mainly constituted by mononuclear cells and sparse eosinophils. Patch testing was performed with the standard series of the Spanish Contact Dermatitis Research Group (GEIDC) and diltiazem at 0.1%, 1%, and 5% in petrolatum. It yielded positive results for cobalt (+), colophonium (+), paraphenylenediamine (++), and PPD mix (+), both at 48 and 96 hr. The patient's sensitivity to metals, hair dyes, and cosmetics had already been studied in the past.

New patch tests with the plants, textile dyes, and rubber (ChemotechniqueR Diagnostics Malmö Sweden) series were performed. They showed a positive reaction, without present relevance, to phenylcyclohexyl-*p*-phenylenediamine (+) and isopropylaminodiphenylamine (+) and a positive reaction with possible present relevance to disperse red 17 (++) , disperse blue 35 (+), 106 (+), and 124 (+).

The patient was recommended to change the colour of her clothes and subsequently the lesions on her forearms improved. However, the photo-induced lesions on the face, V-neck area, and hands persisted.

Then, photopatch tests with 5 J/cm² UVA, including plants series and diltiazem, were performed at the same concentrations used in patch testing. They elicited a positive result for diltiazem 5% (+) at 48 and 96 hr.

The phototest with 5 J/cm² UVB was within the normal range according to the patient's age and cutaneous phototype. Patch test with diltiazem at 0.5%, 1%, and 10% in petrolatum on a control group were negative at 48 and 96 hr.

The patient was finally diagnosed an allergic contact dermatitis to textile dyes and a photoallergic cutaneous eruption due to diltiazem. Her lesions improved substantially since diltiazem was replaced with ramipril.

Discussion

Diltiazem is a calcium channel inhibitor classified in the benzothiazepines group. It has a short half-life and hepatic metabolism (2). Nine of its intermediate metabolites, including desacetyldiltiazem and desmethyl diltiazem, have been identified as inductors of some of the adverse reactions that this drug can cause (3).

The cutaneous manifestations related to diltiazem are diverse (1) and include phototoxic dermatitis (4, 5, 7). The etiopathogenesis of the latter is unknown. Some authors have suggested that some of the metabolites of diltiazem might induce photosensitivity, as the *in vitro* absorption spectrum of diltiazem is not in the UVA ranges, which are responsible of the vast majority of photoinduced drug reactions (4, 6). Diltiazem superoxide has been implied as a possible photoallergen (7).

Epicutaneous patch tests are useful for reinforcing the diagnosis of cutaneous adverse reactions to this drug

(8–10). They are mainly performed with diltiazem "as is" preparations, diltiazem at 1%, 5%, 10%, 20%, and 30% in petrolatum preparations, diltiazem at 5%, 10%, 20%, and 30% in water preparations, and diltiazem at 30% in alcohol preparations (8–10).

Given the fact that in some instances the cutaneous lesions do not clinically improve after replacing the suspected calcium channel antagonist with a different one, cross-reactions among these drugs are being considered (9, 10). Cholez et al. divided calcium channel inhibitors into two main groups: dihydropyridines (nifedipine) and no-dihydropyridines (verapamil and diltiazem) and considered cross-reactions among drugs from different groups to be uncommon (9).

To our knowledge, no other photoallergic eruptions related to diltiazem have been reported in the literature. The patient we describe showed a concomitant sensitization to dyes, but it could not explain itself the photodistributed cutaneous lesions. Furthermore, both the patient's significant clinical improvement after replacing diltiazem and the positive results of the patch testing enhance our diagnosis.

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