

Strong reactions to diltiazem patch tests: Plea for a low concentration

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Diltiazem is known to induce cutaneous adverse drug reactions (CADRs). Patch tests are sensitive tools for diagnosis of CADRs.^{1,2} We herein report diltiazem-induced CADRs in three women in their 60s with severe reactions to the patch test and discuss the concentration to use.

1 | CASE REPORTS

Case 1 was patch tested 6 weeks after acute generalized exanthematous pustulosis (AGEP) with diltiazem 10% pet. (Chemotechnique Diagnostics, Vellinge, Sweden) and diltiazem pills brought in by the

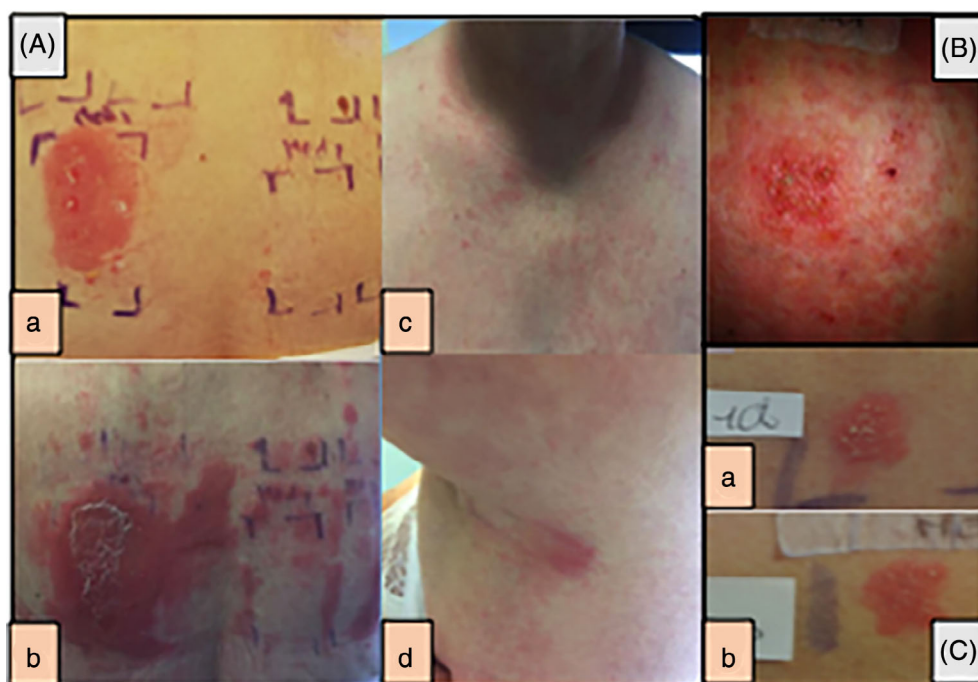


FIGURE 1 (A) Case 1: (a) +++ patch test reaction on day 2 (D2) with 3% diltiazem obtained from pills diluted at 30% in pet. and diltiazem 10% pet.; (b) angry back reaction on D4; (c, d) maculopapular exanthema on D4. (B) Case 2: diltiazem 10% pet. yielding +++ reaction and large involvement of the back on D4. (C) Case 3: (a) pustular reaction to diltiazem 10% pet. on D4; (b) pustular reaction to diltiazem 3% pet. on D4

patient, diluted at 30% in pet. with a final concentration of 3% pet. The PTs were applied to the unaffected upper back skin for 2 days, using IQ chambers (Chemotechnique Diagnostics), with readings obtained on Day 2 (D2) and D4.¹ On D2 the patch test results were +++ and on D4 she developed an angry back reaction associated with maculopapular exanthema (MPE) involving her face, neck, and armpits, without systemic symptoms. Case 2 did not provide her own drug so she was only patch tested with diltiazem 10% pet., 4 months after an MPE episode. The patch test result was +++ on D2, spreading widely on her back on D4. Case 3 was patch tested with diltiazem 10% pet. and 3% pet., as the first patient, 3 months after an AGEF episode. Patch test results were ++ on D2 and became pustular on D4 (Figure 1 and Online supplemental Table 1).

2 | DISCUSSION

We report three cases of strong to extreme reactions to patch tests with diltiazem, including one with a relapse of MPE of moderate severity. Diltiazem is known to induce CADR including MPE, AGEF, and drug reaction with eosinophilia and systemic symptoms.^{3,4} Patch testing with diltiazem is known to be useful for the diagnosis of diltiazem-induced CADR.³⁻⁵ The guideline recommendations for drug PTs are to use the pure drug diluted at 10% or the commercialized form of the drug diluted at 30%, no matter which drug is to be tested.¹ However, some drugs such as carbamazepine or hydroxyzine require lower concentrations of the pure drug for patch testing. In current practice, it is possible and easy to use the ready-to-use syringes of Chemotechnique Diagnostics, and currently the concentration for diltiazem is 10% pet. In our department, when available, we also test the own drugs of the patients diluted at 30% pet., that is, a final concentration of 3% of pure drug for diltiazem.⁵ Numerous positive PT results with a concentration of diltiazem from 0.1% to 1% have already been published as well as several generalized MPE after anal application of a 2% diltiazem cream.³⁻⁷ According to our CADR cases, those reported in the literature, and the generalized reactions seen after localized application of the cream, use of a low concentration of diltiazem for PT when this drug is suspected to be the culprit is suggested, namely, if possible, 1% instead of 10% of pure

diltiazem, and otherwise not more than 3% concentration, which is obtained by diluting the marketed form at 30%, as used in the present cases.⁵

CONFLICTS OF INTEREST

The authors declare no potential conflict of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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Online supplemental Table: Patch-tests results in the three patients:

Patch-test	Diltiazem concentration	Case 1 D2/D4	Case 2 D2/D4	Case 3 D2/D4
PT10	10% pet. Chemotechnique Diagnosis	+++:/angry back and MPE	+++:/extensive reaction of the back	++/pustular reaction
PT3	Pills diluted 30% pet. (3% final concentration)	+++:/angry back and MPE	Not done	++/pustular reaction

PT10: PT with 10% pet. diltiazem,(Chemotechnique Diagnosis) ; PT3: PT with diltiazem tablets diluted to 30% in pet. with a final concentration of 3% ; MPE: maculopapular exanthema