

CONTACT POINTS

CONTACT DERMATITIS 2010: 63: 228–232

• JOHN WILEY & SONS A/S 2010

• ALL RIGHTS RESERVED

• CONTRIBUTIONS TO THIS SECTION WILL NOT UNDERGO PEER REVIEW, BUT WILL BE REVIEWED BY THE EDITOR •

Contact allergy to diltiazem cream

Contact Dermatitis 2010: 63: 228–230

P. T. Leinonen^{1,2}, R. Riekkilä¹ and
A. Oikarinen¹

¹Department of Dermatology, University of
Oulu, Oulu 90014, Finland and ²Department
of Anatomy and Cell Biology, Institute of
Biomedicine, University of Oulu 90014,
Oulu, Finland

Key words: contact allergy; calcium channel
blocker; diltiazem.

Introduction

Systemically applied calcium channel blockers, such as diltiazem, verapamil, amlodipine, felodipine, lacidipine, lercanidipine, nicardipine, nifedipine, nimodipine, and nitrendipine, are widely used to lower blood pressure. They block voltage-gated calcium

channels in the muscle walls of the arteries, leading to relaxation of the vessels and lower blood pressure. Topical calcium channel blocker creams are used to treat anal fissures and Raynaud's syndrome. Topical administration of calcium channel blocker cream is antipruritic, and relieves ischaemia by relaxing the muscles and dilating small blood vessels in the affected areas of skin.

Several reports have been published of delayed hypersensitivity reactions to systemic calcium channel blockers. One case report has described contact allergy to topical calcium channel blocker cream. We present here another novel case with verified contact allergy to topical diltiazem.

Case History

Our patient is a 53-year-old woman suffering from asymptomatic extrasystolic beats treated with β -blockers when needed. She regularly used calcium, vitamin D, and an oral contraceptive. Over 2007–2009, the patient had anal fissures, which were repeatedly treated with 2% diltiazem cream (Table 1).

The patient was referred to our clinic because she had developed localized skin irritation and eczema in the anogenital area. Over several months, the skin symptoms worsened and spread to the lower body. The patient was examined for allergies with the baseline series and cosmetic series, with no allergic reaction. Because the symptoms were relieved when the use of diltiazem cream was discontinued, the patient was subjected to a diltiazem cream use test, with a highly positive result. A use test with plain cream without diltiazem did not show any reaction. The patient was further subjected to a patch test

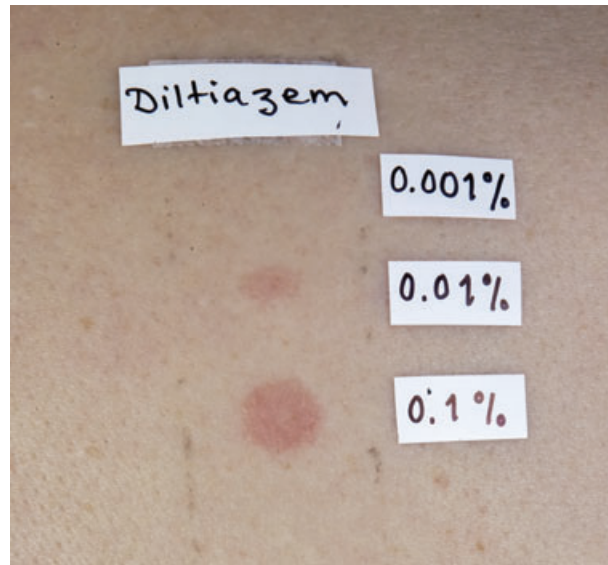


Fig. 1. Positive reactions to 0.1% and 0.01%, but not to 0.001%, diltiazem.

for diltiazem, which gave a positive reaction for 0.1% and 0.01%, but not for 0.001%, diltiazem (Fig. 1). The diltiazem concentrations used were also tested on 21 control persons, with no positive reactions (data not shown).

Discussion

Oral calcium channel blockers may induce a generalized cutaneous reaction (1), erythema, fever and angioedema (2), psoriasiform reaction (3), maculopapular reaction (4), photoallergic dermatitis (5), and reversible hyperpigmentation (6). In these cases, the patch test result is often positive when the reaction is induced by diltiazem, but more rarely with other calcium channel blockers (3). Therefore, patch tests would be useful in diagnosing a cutaneous reaction to diltiazem, but not necessarily to other calcium channel blockers.

Some evidence also implies that there is cross-reactivity in patch tests between different calcium channel blockers (7). Whether or not this has clinical relevance has not been determined, but, until further information becomes available, it is advisable to avoid all calcium channel blockers if an adverse cutaneous reaction to a calcium channel blocker has been confirmed. On the other hand, systemic (8) or topical (9) calcium channel blockers have been reported to be able to diminish contact dermatitis symptoms following chloro-2,4-dinitrobenzene application in a mouse model.

At present, little is known about contact allergies connected with calcium channel blockers. One case report has described topical administration of the calcium channel blocker diltiazem inducing skin eruption, with a confirmed patch test reaction (10). However, the diltiazem concentration used in the patch test was notably high (50% pet.), which may also cause irritation, as seen in two control persons. Our present report describes a similar contact allergy reaction following diltiazem cream treatment. Our patient developed an allergic reaction to 0.01% diltiazem, which was not seen in any of the controls. These results confirm that contact allergy to calcium channel blockers exists, although it seems to be relatively rare as compared with delayed hypersensitivity reactions to systemic calcium channel blockers.

Conflicts of interest: The authors have declared no conflicts.

Table 1. Two per cent diltiazem cream

Ingredients	Concentration (%) (wt/wt)
Diltiazem	2
Novalan®	98
Aqua*	—
PEG-8*	—
Petrolatum*	—
Cetearyl alcohol*	—
Ceteth-20*	—
Sodium cetearyl sulfate*	—
Methylparaben*	—

*Part of a commercial cream, Novalan®.

References

1. Sousa-Basto A, Azenha A, Duarte M L, Pardal-Oliveira F. Generalized cutaneous reaction to diltiazem. *Contact Dermatitis* 1993; 29: 44–45.
2. Romano A, Pietrantonio F, Garcovich A, Rumi C, Bellocchi F, Caradonna P, Barone C. Delayed hypersensitivity to diltiazem in two patients. *Ann Allergy* 1992; 69: 31–32.
3. Kitamura K, Kanasashi M, Suga C, Saito S, Yoshida S, Ikezawa Z. Cutaneous reactions induced by calcium channel blocker: high frequency of

- psoriasiform eruptions. *J Dermatol* 1993; 20: 279–286.
4. Cholez C, Trechot P, Schmutz J L, Faure G, Bene M C, Barbaud A. Maculopapular rash induced by diltiazem: allergological investigations in four patients and cross reactions between calcium channel blockers. *Allergy* 2003; 58: 1207–1209.
 5. Ramirez A, Perez-Perez L, Fernandez-Redondo V, Toribio J. Photoallergic dermatitis induced by diltiazem. *Contact Dermatitis* 2007; 56: 118–119.
 6. Kuykendall-Ivy T, Collier S L, Johnson S M. Diltiazem-induced hyperpigmentation. *Cutis* 2004; 73: 239–240.
 7. Gonzalo Garijo M A, Perez Calderon R, De Argila Fernandez-Duran D, Rangel Mayoral J F. Cutaneous reactions due to diltiazem and cross reactivity with other calcium channel blockers. *Allergol Immunopathol (Madr)* 2005; 33: 238–240.
 8. Diezel W, Gruner S, Anhalt G J, Strunk D, Shanks M, Sonnichsen N. Contact hypersensitivity (DNCB test) and inhibition by the calcium channel blocker diltiazem. *Dermatol Monatsschr* 1989; 175: 170–174.
 9. Wille J J, Kydonieus A, Kalish R S. Several different ion channel modulators abrogate contact hypersensitivity in mice. *Skin Pharmacol Appl Skin Physiol* 1999; 12: 12–17.
 10. Rose R F, Wilkinson S M. Contact sensitization to topical diltiazem. *Contact Dermatitis* 2009; 60: 347–348.

Address:

P. T. Leinonen

Department of Dermatology

University of Oulu

PO Box 5000

Oulu 90014

Finland

Tel: +358 83153508

Fax: +358 83153135

e-mail: pekka.t.leinonen@oulu.fi