Contact Dermatitis from Nitroglycerin in a Transdermal Therapeutic System

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Sir,

Nitroglycerin has been in use for relief of angina for more than 100 years, but allergic reactions to it or to other organic nitrates rarely feature in the medical literature. Most such reactions are irritative contact dermatitis caused by nitroglycerin in the form of both ointments (1) and transdermal therapeutic systems (TTS) (2).

CASE REPORT

A 62-year-old woman developed pruritus, oedema, erythema and vesiculation, well demarcated at the application sites of nitroglycerin TTS on the trunk and upper arms (Fig. 1). Lesions healed with post-inflammatory hyperpigmentation. Two weeks before, the patient had started treatment for coronary insufficiency with daily nitroglycerin transdermal patches (Dermatrans 5®, Recordati group, Madrid, Spain), and 6 days later she noted pruritus. The symptoms started 12 h after rechallenge. Although the patches were substituted with another brand, the pruritus and eczema did not decrease. Nitroglycerin TTS was withdrawn and the patient was treated with topical corticosteroids and oral antihistamines for a week. Later, patch tests were carried out with adhesives and nitroglycerin 1%, 0.5% and 0.1% in petrolatum (Fig. 2). All the nitroglycerin patch tests were positive at 48 h (stronger) and at 72 h, but the adhesive proved negative. The woman subsequently received sublingual nitroglycerin without adverse effects. Furthermore, the patient had been on isosorbide mononitrate orally for the last year because she had high blood pressure, but no cross-sensitivity allergic reaction occurred.

DISCUSSION

Transdermal nitroglycerin is commonly used, but may induce contact dermatitis. The frequency of adverse skin reactions is controversial and may vary from 10% to 75% according to different authors. These cases of contact dermatitis are mainly irritant reactions. Irritation can be due to an immediate second application of the TTS patch, over the same skin area, without a patch-free interval. The occlusive patch can cause accumulation of sweat with subsequent plugging of the sweat ducts. The skin irritations are non-specific reactions and are characterized by erythema and induration, maximal at the margins with sharp line demarcation corresponding to the site of application of the patch. Their frequency may diminish with the incorporation of hydrogels that absorb water, and with chlorhexidine pre-treatment that decreases bacterial overgrowth under the disc (2).

Although nitroglycerin is a sensitizing agent, and allergic skin reactions may occur in response to topically applied nitroglycerin, allergic contact dermatitis from nitroglycerin TTS is very rare. Lesions are generally limited to the application site, but in the literature generalized reactions from nitroglycerin TTS, such as

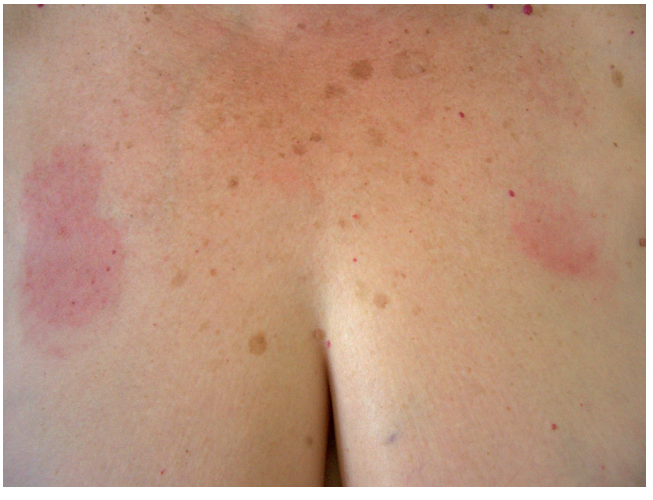

Fig. 1. Well-demarcated acute eczema at the application sites of a nitroglycerin transdermal therapeutic system.

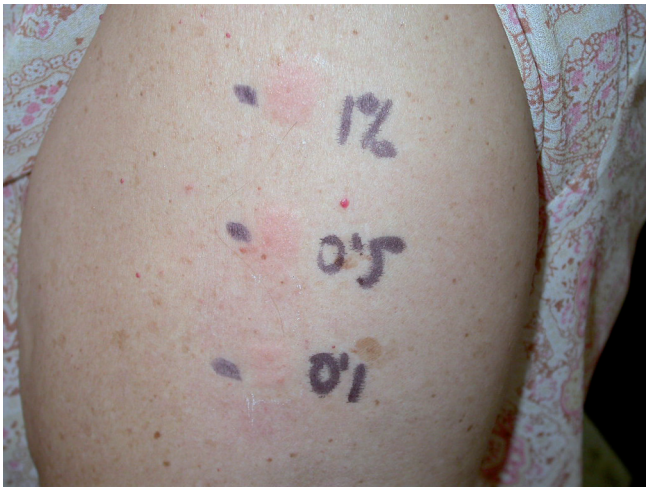

Fig. 2. Patch test at 72 h after applying various concentrations of nitroglycerin.

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generalized allergic contact dermatitis (3) or erythema multiforme (4), have been described. This can occur if discontinuation of the use of nitroglycerin TTS is not carried out promptly (3).

The diagnosis is based on the patch test. The concentrations and vehicles suggested in the literature for patchtesting are nitroglycerin 0.01% to 2% in petrolatum, 0.2–0.5% in water or ethanol. As nitroglycerin is difficult to handle because it is flammable, in some reported cases, nitroglycerin allergy has been proven by application of various commercial preparations of nitroglycerin in different excipients (5). A positive reaction should lead to oral challenge testing in a hospital. Usually, oral and sublingual provocation do not produce any reactions, but a cross-sensitivity allergic reaction to nitroglycerin and isosorbide dinitrate has been described (6).

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