Contact dermatitis from Nitroderm

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Key words: transdermal delivery system; nitroglycerin; allergic contact dermatitis; medicaments.

Case Report

A 58-year-old man with a medical history of myocardial infarction 5 years earlier, and since then under therapy with oral nitrates, had been changed in February 1987 to using a transdermal delivery system for nitroglycerin, Nitroderm TTS 10 (Ciba-Geigy), every 24 h. After 13 months, the patient developed a pruritic erythematous vesicular eruption at the site of the delivery system application (site correctly changed every time). Nevertheless, the patient went on with the application until 20 days before hospitalization.

On examination, all his body, with the exception of the head and the extremities of limbs, showed erythematous vesicular lesions, some isolated, some forming scaly scabby patches, with itching; on his chest, we observed some brown-red patches several cm in length (Fig. 1).

Because of the severity of the cutaneous reaction, the patient was treated with systemic steroid. After 2 weeks of this therapy, he improved, but the brown-red patches on the chest were still visible. His cardiologic therapy was changed to another nitrate (isosorbide-5-mononitrato, Ismo-20) 2 tablets a day, without recurrence of angina.

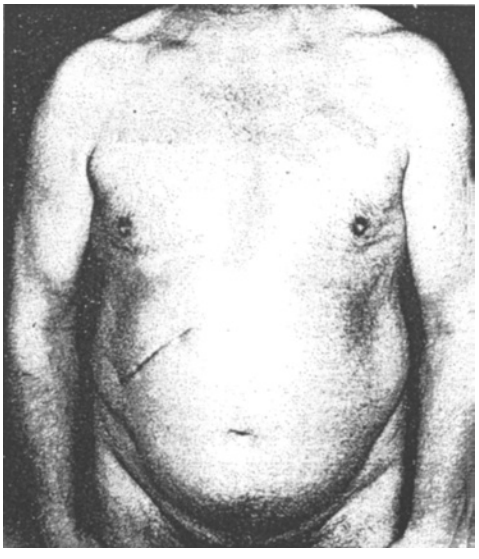

Fig. 1. Brown-red patches and diffuse erythematous vesicular lesions over the chest and abdomen.

6 weeks later, the patient was tested with Nitroderm TTS 10 system in toto, applied to the left upper chest (where there were no brown-red patches), and with the GIRDCA standard series. After 72 and 96 h, we noticed a strong erythematous vesicular (+++) reaction at the site of Nitroderm TTS 10 application, while the GIRDCA standard series was negative.

Patch tests with nitroglycerin 0.5, 1, 2 and 3% pet. gave negative results. To another site, we also applied a placebo device of Nitroderm (Nitroderm-Placebo, lactose 500 mg) and a single component of the adhesive layer, polydimethylsiloxane, also with negative results.

Discussion

Despite its wide use, allergic contact dermatitis from transdermal therapeutic systems for nitroglycerin is very rare. Bressler (1) in 1949 and Einert et al. (2) in 1963 reported cases of nitroglycerin reaction in pharmaceutical workers; subsequently there were some papers about allergic contact dermatitis from nitroglycerin ointment (3–5).

In 1983, Camarasa & Perez (6) reported the results of patch tests with nitroglycerin in 22 patients under therapy with oral nitroglycerin, showing sensitivity in only one of them. Other studies on TTS nitroglycerin demonstrated that contact dermatitis from this compound is a rare event (7, 8).

Letendre et al. (9) recently reported an adverse dermatologic "burn-like" reaction to transdermal nitroglycerin, probably due to the delivery system rather than to nitroglycerin. Finally, Harari et al. (10) published a case of contact dermatitis from nitroglycerin, with post-inflammatory hypermelanosis at the site of reaction, where the patient reacted to nitroglycerin (+++), as well as to its delivery device (+).

Over the past few years, other drugs have been incorporated into transdermal delivery systems (clonidine, scopolamine, estradiol, testosterone). Schwartz & Clendenning (11) reported a case of allergic contact dermatitis from hydroxypropyl cellulose in a transdermal estradiol patch.

Holdiness (12) has recently published a review of contact dermatitis associated with the above-mentioned transdermal delivery systems, which noted that clonidine had the highest % of contact dermatitis. With regard to nitroglycerin, contact allergy had rarely been demonstrated. He concluded that the drug, vehicle or adhesive system leads to contact dermatitis, but that none of the agents suspected of being formed during the manufacturing process had been identified (12).

Our case is like that of Letendre et al. (9): negative to nitroglycerin, but positive (+ + +) to the system in toto. We think that the system is responsible for allergic contact dermatitis because of its complex composition. The nitroglycerin adsorbed on lactose is in fact in a medical silicone fluid, with colloidal silicone added to increase the viscosity: the rate-controlling membrane is made of ethylene vinyl acetate copolymer. One of these agents could be responsible for the cutaneous reaction, but we have not patch tested with all the separate components, as did other authors (10).

The negativity to Nitroderm placebo, as well as to nigroglycerin, leads us to believe that the system in toto is responsible for the allergic reaction, which we could still see 3 months after the first patch test. The other nitrate, isosorbide-5-mononitrato, which replaced the transdermal therapy, has so far provoked no reaction.

In the future, more cases of contact dermatitis will be seen, as transdermal delivery systems are used more commonly. Either the drug or the vehicle can cause allergic contact dermatitis, because both have allergic potential. Considering the negative results to nitroglycerin, we can hypothesize that one or more of the components of the transdermal delivery system are responsible of the cutaneous reaction experienced by our patient.

Acknowledgement

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References

1. Bressler R R. Nitroglycerin reactions among pharmaceutical workers. *Ind Med Surg* 1949: *18:* 519–523.
2. Einert C, Adams W, Crothers R et al. Exposure to a mixture of nitroglycerin and ethylene glycol dinitrate. *Am Ind Hyg Ass J* 1963: *24:* 435–447.
3. Sauker W F, Frederick F D F. Allergic contact dermatitis secondary to topical nitroglycerin. *J Am Med Assoc* 1978: *239:* 1743–1744.
4. Hendricks A A, Dec W. Contact dermatitis due to nitroglycerin ointment. *Arch Derm* 1979: *115:* 853–855.
5. Chandraratna P A N, O'Dell R E. Allergic reactions to nitroglycerin ointment: report of 5 cases. *Curr Therap Res* 1979: *25:* 481–484.
6. Camarasa J G, Perez M. Nitroglycerin sensitivity. *Contact Dermatitis* 1983: *9:* 320–321.
7. Fisher A A. Dermatitis due to transdermal therapeutic systems. *Cutis* 1984: *34:* 526–531.
8. Topaz O, Abraham D. Severe allergic contact dermatitis secondary to nitroglycerin in a transdermal therapeutic system. *Ann Allergy* 1987: *59:* 365–366.
9. Letendre P W, Barr C., Wilkens K. Adverse dermatologic reaction to transdermal nitroglycerin. *Drug Intell Clin Pharm* 1984: *18:* 69–70.
10. Harari Z, Sommer I, Knobel B. Multifocal contact dermatitis to Nitroderm TTS-5 with extensive postinflammatory hypermelanosis. *Dermatol* 1987: *174:* 249–252.
11. Schwartz B K, Clendenning W E. Allergic contact dermatitis from hydroxypropyl cellulose in a transdermal estradiol patch. *Contact Dermatitis* 1988: *18:* 106–107.
12. Holdiness M R. A review of contact dermatitis associated with transdermal therapeutic systems. *Contact Dermatitis* 1989: *20:* 3–9.

Contact dermatitis from myoelectric prostheses

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Key words: allergic contact dermatitis; myoelectric prostheses; upper limb stump; nickel; phenol formaldehyde resin; diaminodiphenylmethane; phenylglycidyl ether; plastics.

Allergic contact dermatitis may affect the skin of an amputated limb as a result of prolonged occlusive contact with the prosthesis socket material (1–3). Previously reported cases (2, 4–10) refer to forelimb prostheses.

The cases we observed between November 1987