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Fenofibrate photoallergy – relevance of patch and photopatch testing

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Fenofibrate is one of the most frequently prescribed drugs for the treatment of hyperlipidaemia (1, 2). Although cutaneous adverse reactions attributed to the drug occur in ~2% of patients, photosensitivity is assumed to be rare (1, 2).

Case Report

A 60-year-old non-atopic woman presented with an eczematous eruption on the face, V-area of the neck, forearms, and backs of the hands (Fig. 1) associated with itching and burning, highly suggestive of photosensitivity. This skin eruption appeared 2 weeks after she had starting using Catalip 267 micronizado[®] capsules (fenofibrate, 267 mg daily) for the treatment of hypertriglyceridaemia. The patient denied previously using any topical product containing ketoprofen for analgesia. Oral prednisolone 0.5 mg/kg/day, ebastine 10 mg/day, topical hydrocortisone and betamethasone dipropionate cream were given, and fenofibrate was stopped, resulting in complete resolution of the rash. Three months later, patch and photopatch tests with IQ UltraTM chambers (Chemotechnique Diagnostics, Vellinge, Sweden) applied on the back and covered with Mefix[®] (Mölnlycke Health Care, Göteborg, Sweden) were performed with the Portuguese baseline series and the European photopatch test baseline series, respectively, all from Chemotechnique. As recommended by the photopatch test taskforce group, in order to clarify photopatch reactions to ketoprofen, patch testing with cinnamyl alcohol was performed simultaneously. Photopatch tests were carried out by applying



Fig. 1. Eczematous eruption on the face and V-area of the neck.

the allergens on one side of the back for 48 h, and exposing them to ultraviolet (UV) A at a dose of 5 J/cm² (UV 7001 K; Waldmann, Villingen-Schwenningen, Germany); the opposite site of the back was covered with a black cloth. Readings were performed on day (D) 2, D4 and D7 according to ESCD guidelines. Patch tests gave positive reactions to cinnamyl alcohol (++ on D2, D4, and D7), and photopatch tests showed photoallergy, with the following responses in the irradiated set only: fenofibrate +++, ketoprofen +++, and octocrylene + (all on D4 and D7).

Discussion

The photosensitizing capacity of fenofibrate is mainly determined by the photoexcited chemical structure, the benzophenone moiety, which has also been shown to be responsible for the photosensitizing properties of some other drugs, such as ketoprofen (1, 2, 5). This fact explains

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the high prevalence of cross-photosensitization between these drugs, as observed in the reported case. Photosensitization to ketoprofen leads, in many cases, to photocontact allergy to the UV absorber octocrylene (3). The mechanism of this reaction is unknown, as ketoprofen and octocrylene appear to have little structural similarity, and as octocrylene does not have the benzophenone substructure (3). However, aminolysis and hydrolysis of octocrylene in the skin may lead to the production of benzophenone, so the frequent co-reactivity to octocrylene might also be explained as cross-sensitivity (3). In the present case, it is possible, but not certain, that the positive reactions to ketoprofen and octocrylene were attributable to cross-reactions with fenofibrate. Moreover, a strong association with sensitization to cinnamyl alcohol has been detected in patients with contact photoallergy to ketoprofen (4). The mechanisms responsible for this cross-reactivity are still unknown, although some

hypotheses have been proposed, such as structural similarities or the formation of common metabolites (4, 5).

The use of photopatch testing in clinical practice in the diagnosis of photo-induced drug eruptions is largely limited to testing for topically applied medications. Its use for the diagnosis of photo-induced cutaneous eruptions caused by systemic medication has not been validated (6). This case shows not only this rarely reported adverse effect of fenofibrate, but also that patch and photopatch testing may have a place in the study of systemic photosensitivity dermatitis.

Cross-sensitivity and co-reactivity between fenofibrate, ketoprofen, octocrylene and cinnamyl alcohol should be further investigated, in order to address the need to avoid these substances, and to provide better advice to allergic patients regarding the prevention of recurrences of photocontact and contact dermatitis from this source.

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