Contact Point

Three additional cases of facial allergic contact dermatitis from the powerful pigment-lightening agent phenylethyl resorcinol

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To date only three cases of allergic contact dermatitis (ACD) from the relatively new and potent skin-lightening agent phenylethyl resorcinol (PER) have been reported (1, 2). We describe three additional cases of severe ACD from this substance contained in pigment-lightening cosmetics.

Case Reports

Case 1

A 42-year-old non-atopic woman of Mediterranean origin presented to the UCL Dermatology Department in Brussels with a 3-month-history of itchy, erythematous plaques on cheeks and eyelids. As ACD was suspected, patch tests were performed to the European baseline series and a cosmetic series (Chemotechnique Diagnostics, Vellinge, Sweden, and AllergEAZE, SmartPractice, Phoenix, AZ), as well as to her own cosmetics. Following an occlusion of 2 days, the tests were read on day (D)2 and D4 according to International Contact Dermatitis Research Group (ICDRG) criteria. Only a positive reaction (+ and ++, respectively) was observed to Pigmentclar UV with sun protection factor (SPF) 30 (La Roche-Posay, L'Oréal, Clichy, France). Subsequently, additional patch tests were performed with a photopatch test series and with the individual ingredients of the culprit cosmetic, the latter kindly provided by the manufacturer. Readings on D2 and D4 were only positive (both +) to PER 0,5% pet.(**Figure 1A**). Patch tests to PER 0.5% pet. in 10 control subjects gave negative results.

Cases 2 and 3

Two non-atopic Caucasian women, aged 45 and 43 respectively, presented at the UZA Dermatology Department in Antwerp because of a suspicion of ACD from the use of similar skin-lightening products. The first patient suffered from periocular eczema following the

prolonged use of Pigmentclar eye serum, whereas the second patient had developed a severe and oozing facial dermatitis following the application of the same cream as used by the patient in Case 1 (**Figure 1B**). Both patients were eventually patch-tested, in a similar way as Case 1, and readings showed, on D4, strong positive patch test reactions to the culprit products (++ and +++ in the first and second patient, respectively). Additional patch tests to PER 0.3% in an aqua/ethanol mixture (50/50), obtained as an ingredient of the eye serum, confirmed contact allergy to this substance in both patients (+ and ++ on D4, respectively). Both patients also had positive patch test reactions to fragrances, explaining previous episodes of ACD from fragranced products; however, these reactions were not considered relevant for the current ACD from the skin-lightening cosmetics as these were unscented.

Discussion

Allergic contact dermatitis (ACD) from skin-lightening and depigmenting agents to treat melasma and related skin pigmentation disorders is well-known (3-6). Hydroquinone, first used during the 1960s (7), is since 2000 no longer allowed in skin-lightening cosmetics in the EU (8). Therefore, new skin-lightening agents have been developed, such as PER, the latter being a synthetic compound derived from natural lightening compounds found in *Pinus sylvestris* (1). Given its clinical effectiveness (9), it is incorporated in several cosmetics, including sunscreens, pigment-lightening cosmetics and hair-lightening products. PER acts as a potent inhibitor of melanin synthesis by inhibiting tyrosinase, which is the most effective way to reduce hyperpigmentation (10). However, comparatively to other depigmenting agents, such as kojic acid, arbutin and hydroquinone, PER is a more potent inhibitor of human tyrosinase (10) and only few cutaneous adverse reactions have been attributed to it so far. Nevertheless, the use of PER in cosmetics is not without risk. In 2013, Gohara et al. (1) reported the first (Japanese) case of ACD to PER contained in a skin-lightening essence, despite its use in

cosmetics since 2000 in this country. In 2016, Pastor-Nieto et al. described two more (Spanish) cases of ACD to PER contained in a sunscreen (2). Although people with a darker skin complexion more frequently use products containing bleaching agents, and might thus be more prone of developing ACD in this regard (2), we show that anyone using such products may be at risk of developing contact allergy from them.

References

1. Gohara M, Yagami A, Suzuki K, *et al*. Allergic contact dermatitis caused by phenylethyl resorcinol 4-(1-phenylethyl)-1,3-bencenediol], a skin-lightening agent in cosmetics. Contact Dermatitis. 2013;69:311-322.

2. Pastor-Nieto M.A, Sánchez-Pedreño P, Martínez-Menchón T, *et al.* Allergic contact dermatitis caused by phenylethyl resorcinol, a skin-lightening agent contained in a sunscreen. Contact Dermatitis. 2016;75:250-253.

3. García-Gavin J, González-Vilas D, Fernández-Redondo V, *et al*. Pigmented contact dermatitis due to kojic acid. A paradoxical side effect of a skin lightener. Contact Dermatitis. 2010;62:63-64.

4. Matsuo Y, Ito A, Masui Y, *et al*. A case of allergic contact dermatitis caused by arbutin. Contact Dermatitis. 2015;72:404-405.

5. Numata T, Tobita R, Tsuboi R, *et al*. Contact dermatitis caused by arbutin contained in skin-whitening cosmetics. Contact Dermatitis. 2016;75:187-8.

6. Barrientos N, Ortiz-Frutos J, Gómez E, *et al*. Allergic contact dermatitis from a bleaching cream. American Journal of Contact Dermatitis. 2001;12:33-34.

7. O'Donoghue J.L. Hydroquinone and its analogues in dermatology - a risk-benefit viewpoint. Journal of Cosmetic Dermatology. 2006;5:196-203.

8. Twenty-fourth Commission Directive 2000/6/EC. Official Journal of the European Union 2000; L56: 42-6.

9. Vielhaber G, Schmaus G, Jacobs K*, et al.* 4-(1-Phenylethyl)-1,3-benzenediol: a new, highly efficient lightening agent. International Journal of Cosmetic Science. 2007;29:63-66.

10. Kolbe L, Mann T, Gerwat W, *et al*. 4-n-butylresorcinol, a highly effective tyrosinase inhibitor for the topical treatment of hyperpigmentation. Journal of the European Academy of Dermatology and Venereology. 2013;27:19-23.