

Polyhexamethylene biguanide in wound care products: a non-negligible cause of peri-ulcer dermatitis

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Case Report

A 59-year-old non-atopic woman with a long history of bilateral leg ulcers and multiple contact allergies (iodine, cetyl alcohol, limonene, and linalool hydroperoxides) presented with acute worsening of her wounds, accompanied by perilesional eczema. Moreover, she had noticed the occurrence of mild hand dermatitis. She had been cleaning the leg wounds herself daily with Prontosan[®] Wound Irrigation Solution (B. Braun Medical, Boulogne-Billancourt, France), a liquid wound cleanser containing polyhexamethylene biguanide (PHMB, or polyhexanide). Subsequently, she applied

Prontosan[®] wound gel. Skin problems had started to appear after a few days. A repeated open application test (ROAT) with the gel applied twice daily in an elbow fold produced a positive reaction after 10 days. According to the information leaflets of both products, Prontosan liquid and gel contain 0.1% PHMB, 0.1% undecylenamio-propyl betaine, and water; the gel also contains glycerol and hydroxyethyl cellulose.

A patch test with PHMB 5% aq. (diluted in-house from a 20% aqueous solution obtained from Fagron[®], Uitgeest, The Netherlands) was applied on the upper arm for 2 days at the Wound Care Clinic, and was negative upon removal at D2 but became positive at D4, according to a photograph e-mailed by the patient. One week later, she was seen at the Contact Allergy Unit for additional patch testing with a baseline series, chlorhexidine digluconate 0.5% aq., and the Prontosan[®] gel and liquid 'as is'. Additionally, a repeated patch test with PHMB 2.5% and 5% aq. was performed. All patch test

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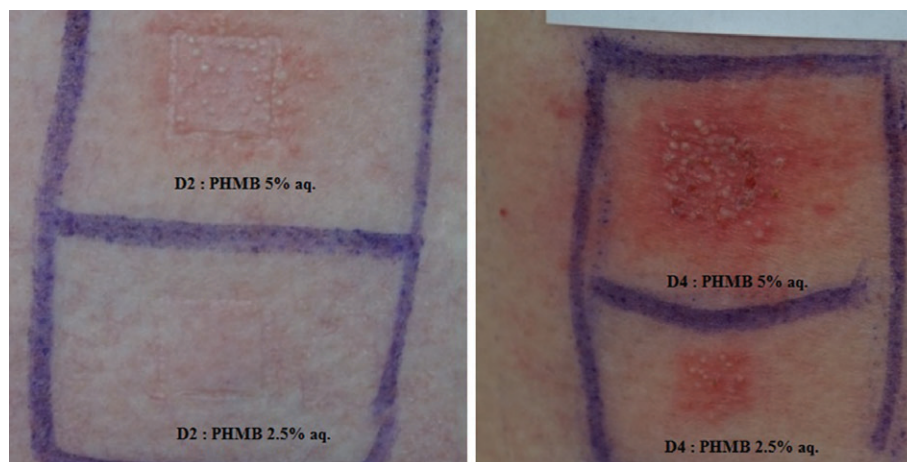


Fig. 1. Reactions to a repeated patch test with polyhexamethylene biguanide (PHMB) 5% aq. and PHMB 2.5% aq. at D2 (left) and D4 (right). Note the pustular aspect.

chambers – also on the first occasion – were from Van Der Bend[®] (Brielle, The Netherlands), and fixation was performed with Fixomull[®] stretch (BSN Medical GmbH, Hamburg, Germany). The tests were again removed after 2 days, and read at D2 and D4, according to ICDRG guidelines.

This time PHMB 5% aq. already gave a positive reaction on D2 (+) and, even more so, on D4 (++), with a partially pustular morphology (Fig. 1). Both the Prontosan[®] liquid and the Prontosan[®] gel gave negative results. Following treatment with topical steroids, and avoidance of PHMB-containing wound care products, the perilesional eczema disappeared and did not recur. Moreover, the hand dermatitis, which was attributed to the Prontosan[®] liquid, also resolved.

Discussion and Conclusion

Polyhexamethylene biguanide (PHMB), or polyhexanide, which belongs to a group of preservatives known as biguanides, and is related to polyaminopropyl biguanide, has been considered to be a rare sensitizer (1). However, the molecule has recently gained attention as a potential cause of both immediate and delayed hypersensitivity, owing to its presence in cosmetics, including wet wipes and make-up removers (2–4). Moreover, a recent Opinion released by the EU Scientific Committee on Consumer Safety stated that PHMB at the presently allowed maximum use concentration of 0.3% in cosmetics cannot be considered safe (5). Although PHMB is related to chlorhexidine, no cross-reactivity, in terms of contact allergy, has been described between PHMB and chlorhexidine, as in the present case, although patients

with immediate-type hypersensitivity to chlorhexidine might be at risk of developing allergy to PHMB (6). In the present case, the patient's history, the positive ROAT result with the Prontosan[®] gel (containing only 0.1% PHMB), the positive patch test reactions to PHMB 2.5% and 5% and the favourable course of both the perilesional eczema and the hand dermatitis following avoidance of PHMB-containing products all suggest a contact allergic mechanism. However, some peculiarities are worth highlighting in this case: (i) the initial patch test with PHMB 5% aq. only gave a positive reaction at D4, whereas retesting with the same substance 1 week later resulted in positive reactions at D2 (+) and D4 (++), which are, in our opinion, explained by a 'booster' effect; (ii) as reported previously (4), products containing only a low concentration of PHMB might give negative test results 'as is', whereas a ROAT with the product and a separate patch test with PHMB at an adequate patch test concentration (e.g. 5% aq.) may confirm contact allergy; and (iii) we observed a partially pustular patch test reaction, which may be explained by the irritant nature of the molecule, although so-called 'pustular patch test reactions' do exist as well, which may be relevant (7), as is also the case in the present report. Likewise, weak patch test reactions might be attributable to the irritant potential of the molecule, but may also represent weak positive reactions (1). At our patch test clinic in Antwerp, we have patch tested PHMB 5% aq. in >50 controls, and we have only rarely observed obviously irritant reactions. According to the literature, 2.5% and 5% are commonly used test concentrations, although the accidental use of a higher test concentration has been reported (2).

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