

Contact dermatitis with clostridiopeptidase A contained in Noruxol[®] ointment

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Caterina Foti, Anna Conserva, Claudia Casulli, Valentina Scrimieri, Maria Luisa Pepe and Domenico Quaranta

Unit of Dermatology, Department of Internal Medicine, Immunology and Infectious Diseases, University of Bari, Policlinico, Piazza Giulio Cesare, 11, I-70124 Bari, Italy

Clostridiopeptidase A, also called collagenase 1, is a proteolytic enzyme capable of

digesting collagen. Preparations containing clostridiopeptidase A are used topically for the debridement of dermal ulcers, burns and other necrotic lesions to facilitate the formation of granulation tissue and subsequent epithelization. We observed 4 patients with a periulcerative eczema after repeated applications of Noruxol[®] ointment (Smith & Nephew Ltd, L Hull, UK). Patch testing with Noruxol[®] ointment as is and its excipients (soft paraffin and white petrolatum), as well as scaled dilutions of the main ingredient of this topical preparation, clostridiopeptidase A (Firma, Florence, Italy), showed doubtful reactions to Noruxol[®] ointment in 3 patients and a positive reactions only in 1 patient. All patients showed positive reactions to clostridiopeptidase A 1% in pet. This study shows the sensitizing capacity of clostridiopeptidase A that should be tested in all patients with suspect sensitization to Noruxol[®] ointment.

Key words: clostridiopeptidase A; contact dermatitis; Noruxol[®]; ulcer.

Clostridiopeptidase A, also called collagenase 1, is derived from fermentation of *Clostridium histolyticum*. Clostridiopeptidase A is a proteolytic enzyme capable of digesting collagen. Preparations containing clostridiopeptidase A are used topically for the debridement of dermal ulcers, burns and other necrotic lesions to facilitate the formation of granulation tissue and subsequent epithelization.

We report 4 cases of allergic contact dermatitis with clostridiopeptidase A contained in an ointment used for treatment of dermal ulcers.

Case Reports

We observed 4 female patients aged 75, 83, 70 and 35 years with ulcerated lower limbs, phlebopathic in nature in the first 2 cases, hypertensive in the third and post-traumatic in the fourth. These patients presented a periulcerative eczema whose onset followed repeated applications of Noruxol[®] ointment (Smith & Nephew Ltd, UK), used regularly for a period ranging from 20 days (D) to 3 months. Suspension of this treatment, together with the administration of topical corticosteroid (mometasone furoate) and systemic antihistamine (levocetirizine), brought about clinical healing. The 4 patients then underwent epicutaneous tests with the standard SIDAPA (Italian Society of Allergological, Occupational and Environmental Dermatology) series, Noruxol[®] ointment as is and its excipients (soft paraffin and white petrolatum), as well as scaled dilutions of the main ingredient of this topical preparation, clostridiopeptidase A (Firma, Florence, Italy). Patch tests were performed using the Al-chambers[™] (Euromedical, Calolziocorte, LECCO, Italy). Readings were made after 2 and 4 D.

The results of patch tests are shown in Table 1. Patients 1, 2 and 4 showed doubtful reactions to Noruxol[®] ointment tested as is and were positive only to clostridiopeptidase A tested 1% in pet. Only in patient 3, there was a clearly positive reaction to Noruxol[®] ointment tested as is and at all the dilutions of clostridiopeptidase A.

Patch tests with clostridiopeptidase A diluted 1% in pet. in 10 healthy volunteers gave negative results.

Table 1. Clinical details and patch test results of the 4 patients

Patient	Age (years)/sex	Site of eczematization	Noruxol [®] ointment as is, D2/D4	Clostridiopeptidase A 1% pet., D2/D4	Clostridiopeptidase A 0.1% pet., D2/D4	Clostridiopeptidase A 0.05% pet., D2/D4	Clostridiopeptidase A 0.001% pet., D2/D4	SIDAPA standard series, D2/D4
1	75/female	Ulcerated lower limbs of a phlebopathic nature	+/-	++	-	-	-	Fragrance mix ++
2	83/female	Ulcerated lower limbs of a phlebopathic nature	+/-	++	-	-	-	-
3	70/female	Ulcerated lower limbs of hypertensive nature	++	++	++	++	++	-
4	35/female	Ulcerated lower limbs of post-traumatic nature	+/-	++	-	-	-	-

Discussion

This study shows the sensitizing capacity of a proteolytic enzyme, clostridiopeptidase A, which is the main component of Noruxol[®] ointment, a topical preparation that is frequently used in Italy in the treatment of skin ulcers and burns.

In literature, only 2 cases of allergic contact dermatitis to Noruxol[®] ointment, tested as is, have been reported (1, 2). In these studies, the sensitizing potential of clostridiopeptidase A, the main component of the preparation, was postulated. However, it is possible that allergic reactions to Noruxol[®] ointment are underestimated, and indeed, 3 of our 4 patients had a doubtful reaction to the topical ointment tested as is (the skin test area showed non-homogeneous papulovesicular lesions scattered over the whole area of application), despite a positive history to periulcerative eczema following use of the product. Instead, in all our patients, positive results were obtained to clostridiopeptidase A diluted 1% in pet. Only 1 subject had a clearly positive result to Noruxol[®] ointment tested as is and at all dilutions of clostridiopeptidase A. To conclude, we can state the sensitizing capacity of clostridiopeptidase A that should be tested in all patients with suspect sensitization to Noruxol[®] ointment. However, we cannot exclude the sensitizing role of secondary proteases (contained in this drug). In fact, the lack of information about these substances has prevented us to perform patch test with them.

Fax: +39 080 5478954

e-mail: c.foti@dermatologia.uniba.it

References

1. Meichlböck A, Bayerl C. Kontaktezem auf Noruxol[®] Salbe bei posttraumatischem Ulkus. *Akt Dermatol* 1999; 25: 272–273.
2. Lisi P, Brunelli L. Extensive allergic contact dermatitis from a topical enzymatic preparation (Noruxol). *Contact Dermatitis* 2001; 45: 186–187.

Address:

Professor Caterina Foti, MD
Unit of Dermatology
Department of Internal Medicine,
Immunology and Infectious Diseases
University of Bari
Policlinico, Piazza Giulio Cesare, 11
I-70124 Bari
Italy
Tel: +39 080 5478996