

Mucocutaneous involvement of the genital and perianal skin during isotretinoin therapy



To the Editor: We read with great interest the letter by Cunningham et al,¹ who drew attention to the effect of isotretinoin therapy, which can lead to vulnerability to injury from frictional forces and, consequentially, effects on the genital and perianal areas.

Isotretinoin acts on the sebaceous glands, reducing their activity; it promotes normalization of keratinization and of tissue matrix metalloproteinase; and it reduces inflammation and *Cutibacterium acnes* growth.² Cheilitis, dry skin, erythema, itching, peeling, bruising, eczematous reactions, conjunctivitis, dry eyes, and eyelid inflammation are the most common adverse effects (>1/10).² However, as reported by Cunningham et al,¹ we also describe in our experience the involvement of the genital region, although patients voluntarily do not report such symptoms.¹

Forty patients in treatment with only isotretinoin (26 female and 14 male patients; mean age, 23.1 years) at our outpatient specific service for acne from February to August 2020 were questioned for the appearance of any effects on the genital area. In particular, 10 of 26 (38%) of female patients reported vulvar dryness, and 7 of 26 (27%) reported dyspareunia. Meanwhile, only 4 of 14 male patients (28%) reported genital dryness; in particular, 2 reported dryness and fissures in the genital area, and 2 reported perianal dermatitis. We noticed that the incidence of this adverse effect was greater in women and in patients receiving therapy at a dosage of 0.6 mg/kg/day for a period of at least of 3 months.

Therefore, we agree with Cunningham et al¹ that it would be useful to include any preventative measures.

Based on clinical evidence, in a previous study, we analyzed the potential capacity of a dietary supplement, based on gamma linolenic acid, vitamin E, vitamin C, beta-carotene, coenzyme Q10, and *Vitis vitifera*, to reduce isotretinoin adverse effects, particularly dry skin, erythema, and desquamation.³

Gamma linolenic acid can increase β -defensin 2 expression by sebocytes, which can give stability to the membrane. In addition, this fatty acid decreases the in vitro expression of keratinocytic proinflammatory cytokines (tumor necrosis factor α , interleukin (IL) 8, and IL-1) and fibroblastic cytokines (IL-8) after ultraviolet B exposure, decreasing dehydration and erythema.^{3,4}

Our data imply that the group of patients receiving therapy with isotretinoin, associated with a dietary supplement, had increased compliance

without a reduction in the therapeutic effectiveness. However, dietary interventions are difficult to prove. Furthermore, there is a lack of consensus on laboratory monitoring for patients on isotretinoin.⁵

Considering the target age group (mainly adolescent and young adults), we believe that is important to preserve interpersonal interactions by eliminating causes of discomfort. We think that the use of similar supplements can be considered an useful strategy in the treatment and prevention of dry skin to increase the adherence to isotretinoin therapy.

In addition, the dryness of the mucosa is a topic of extreme interest during the current COVID-19 era because this virus attacks the airways.

Marianna Donnarumma, MD, Gabriella Fabbrocini, MD, Wanda Lauro, MD, Maria Carmela Annunziata, MD, Maria Ferrillo, MD, and Claudio Marasca, MD

From the Section of Dermatology, Department of Clinical Medicine and Surgery, University of Naples Federico II, Naples, Italy.

Funding sources: None.

Conflicts of interest: None disclosed.

IRB approval status: Not applicable.

Reprints not available from the authors.

Correspondence to: Marianna Donnarumma, MD, Department of Dermatology, University of Naples Federico II, Naples, Italy, Via Pansini 5, 80131 Naples, Italy

E-mail: mavabe@hotmail.it

REFERENCES

1. Cunningham L, Menzies S, Moore E, Shudell E, Moloney FJ, Ralph N. Mucocutaneous adverse effects of the genital and perianal skin from isotretinoin therapy. *J Am Acad Dermatol.* 2020;83:1174-1175.
2. Bagatin E, Costa CS. The use of isotretinoin for acne—an update on optimal dosing, surveillance, and adverse effects. *Expert Rev Clin Pharmacol.* 2020;13(8):885-897.
3. Fabbrocini G, Cameli N, Lorenzi S, et al. A dietary supplement to reduce side effects of oral isotretinoin therapy in acne patients. *G Ital Dermatol Venereol.* 2014; 149(4):441-445.
4. Lee HR, Kim SW, Kim MS, Son SJ, Lee JH, Lee HS. The efficacy and safety of gamma linolenic acid for the treatment of acne vulgaris. *Int J Dermatol.* 2014;53:e199-e200.
5. Tkachenko E, Sharma P, Mostaghimi A. Abnormal baseline lab results rarely lead to treatment modification for patients on isotretinoin. *Dermatology.* 2020;236(6):517-520.

<https://doi.org/10.1016/j.jaad.2020.10.078>