

Topically applied low-dose calcitriol ameliorates atopic eyelid dermatitis



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INTRODUCTION

A negative correlation between vitamin D serum levels and disease severity is increasingly documented in patients with atopic dermatitis (AD), although some contradictory results are reported.¹ In spite of some evidence of beneficial effects of oral vitamin D supplementation in the treatment of AD, no consensus exists on its routine use in this patient group.^{1,2} Although topical application of the vitamin D analogue, calcitriol, at a concentration of 3 µg/g, and its noncalcemic synthetic counterpart, calcipotriol, in an equivalent therapeutic dose of 50 µg/g (= 0.005%), is a safe and effective treatment option for psoriasis,¹ clinical data on this type of treatment in patients with AD are generally lacking.

CASE REPORT

The subject was one of the authors (ST), a 36-year-old man who presented with AD confined to the upper and mainly lower eyelids (Fig 1, A). AD was diagnosed according to the criteria of Hanifin and Rajka.³ The patient had chronically relapsing periorbital dermatitis with pruritus and typical morphology (ie, erythema, fissures, scaling, and lichenification), pronounced itch when sweating, xerosis, seasonal allergic rhinitis with recurrent conjunctivitis, and a family history of atopy. The skin symptoms had lasted over a decade with spontaneous remissions, mainly during summer, and flare-ups during winter seasons. The patient did not report on the use of cosmetics, eye care products, or eye medications suggestive of contact dermatitis. The patient had an insufficient vitamin D (25[OH]D) serum level (22.4 ng/mL), according to the International Endocrine Society.⁴ Initially, he was treated with pimecrolimus cream without any

Abbreviation used:

AD: atopic dermatitis

effects. The skin problem partly resolved by using tacrolimus 0.1% ointment, which reduced the symptoms but for no longer than 1 to 2 weeks after discontinuing the treatment. Finally, a 0.6 µg/g calcitriol cream formulation applied to the affected areas twice a day over 10 days gradually and considerably ameliorated the skin lesions for up to 8 weeks (Fig 1, B). The vehicle of the cream formula did not ameliorate the skin symptoms.

DISCUSSION

Topical vitamin D derivatives are not listed as recommended therapeutic options in evidence-based guidelines for the treatment of AD.⁵ In fact, an unfavorable clinical outcome was described in a case report of a 2-year-old boy whose AD symptoms flared in response to topical application of calcipotriol (0.005%) for a mistaken diagnosis of psoriasis.⁶ In addition, investigations in mouse models found that AD can be induced by topical application of vitamin D₃ analogues at doses corresponding to commercially available calcitriol or calcipotriol preparations used in the therapy of psoriasis patients.^{6,7} Mechanistically, topically applied calcitriol at a concentration of 3 µg/g or its noncalcemic synthetic counterpart, calcipotriol, in an equivalent therapeutic dose of 50 µg/g induced interleukin 4 and thymic stromal lymphopoietin expression in epidermal keratinocytes, both representing pivotal cytokines involved in the pathophysiology of AD.^{6,7} The mechanistic link for the observed difference

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Fig 1. Patient with atopic eyelid dermatitis. **A**, Before and **B**, 10 days after topical calcitriol (0.6 $\mu\text{g/g}$) treatment.

between improvement of skin scores by systemic vitamin D supplementation and the reverse effect through topical vitamin D application in AD patients is widely unclear. Although it is known that vitamin D can exert immunoregulatory effects,¹ a possible stimulation of keratinocytes and dendritic cells by topical application of calcitriol in a commercially available concentration (3 $\mu\text{g/g}$) may override the immunomodulatory action of 1,25-dihydroxyvitamin D₃, thereby promoting a pro-allergic milieu in this disease. In fact, because topically applied calcitriol (0.6 $\mu\text{g/g}$) did not lead to worsening of AD skin symptoms in our case, we speculate that this low-dose treatment did not induce AD-relevant proinflammatory cytokines but rather restored a normal cytokine balance resulting in improvement of the skin lesions. This finding is in line with the assumption of Paracelsus that “All things are poison, and nothing is without poison: the dose alone makes a thing not poison.”

Future studies are needed to confirm our findings in a larger group of AD patients by a more objective evaluation (eg, SCORing index of AD), especially in those with involvement of vulnerable and sensitive areas of the body such as the face for which long-

term treatment with conventional topical corticosteroids is contraindicated.

REFERENCES

1. Umar M, Sastry KS, Al Ali F, et al. Vitamin D and the pathophysiology of inflammatory skin diseases. *Skin Pharmacol Physiol*. 2018;31(2):74-86.
2. Sidbury R, Tom WL, Bergman JN, et al. Guidelines of care for the management of atopic dermatitis: Section 4. Prevention of disease flares and use of adjunctive therapies and approaches. *J Am Acad Dermatol*. 2014;71(6):1218-1233.
3. Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. *Acta Derm Venereol Suppl (Stockh)*. 1980;92:44-47.
4. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2011;96(7):1911-1930.
5. Eichenfield LF, Tom WL, Berger TG, et al. Guidelines of care for the management of atopic dermatitis: section 2. Management and treatment of atopic dermatitis with topical therapies. *J Am Acad Dermatol*. 2014;71(1):116-132.
6. Turner MJ, Dasilva-Arnold SC, Yi Q, et al. Topical application of a vitamin D analogue exacerbates atopic dermatitis and induces the atopic dermatitis-like phenotype in Stat6^{VT} mice. *Pediatr Dermatol*. 2013;30(5):574-578.
7. Li M, Hener P, Zhang Z, et al. Topical vitamin D3 and low-calcemic analogs induce thymic stromal lymphopoietin in mouse keratinocytes and trigger an atopic dermatitis. *Proc Natl Acad Sci U S A*. 2006;103(31):11736-11741.