Topically applied low-dose calcitriol ameliorates atopic eyelid dermatitis

Stefan Tukaj, PhD,[a] Detlef Zillikens, MD,[b] and Michael Kasperkiewicz, MD[b]
Gdańsk, Poland and Lübeck, Germany

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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 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.

Abbreviation used:

AD: atopic dermatitis

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 D_3 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

From the Department of Molecular Biology, Faculty of Biology, University of Gdańsk[a] and the Department of Dermatology, University of Lübeck.[b]

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Correspondence to: Stefan Tukaj, PhD, Department of Molecular Biology, Faculty of Biology, University of Gdańsk, Wita Stwosza 59, 80-308 Gdańsk, Poland. E-mail: stefan.tukaj@biol.ug.edu.pl.

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Fig 1. Patient with atopic eyelid dermatitis. **A**, Before and **B**, 10 days after topical calcitriol (0.6 μg/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 μg/g) may override the immunomodulatory action of 1,25-dihydroxyvitamin D_3, thereby promoting a pro-allergic milieu in this disease. In fact, because topically applied calcitriol (0.6 μg/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.

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