

Combination Therapy of Tetracycline and Tacrolimus Resulting in Rapid Resolution of Steroid-Induced Periocular Rosacea

Anju Pabby, MD; Kathy P. An, MD; Richard A. Laws, MD

Standard treatment of steroid-induced rosacea includes discontinuation of steroids and use of an oral tetracycline. A temporary decrease to a lower-potency steroid prior to discontinuation remains optional. The limitations of standard therapy include a prolonged course of treatment with exacerbations prior to permanent improvement. Our challenge was to identify a treatment regimen to resolve steroid-induced periocular rosacea quickly and with minimal rebound effect.

Cutis. 2003;72:141-142.

Case Report

A 55-year-old man with an unremarkable medical history was referred to us by his physician for a persistent facial rash. The patient had a long-term history of seborrheic dermatitis that had been treated for approximately the previous 12 months with fluticasone cream twice a day.

Results of the patient's physical examination revealed background erythema and telangiectasias with 1- to 3-mm discrete erythematous papules (Figure 1). The history and physical examination of the facial rash was most consistent with steroid-induced periocular rosacea.

The use of the fluticasone cream was discontinued, and the patient was started on tacrolimus 0.1% ointment twice a day for 3 weeks and oral tetracycline 500 mg twice a day.

The patient reported improvement several days after starting therapy. At the 3-week follow-up visit, we noted marked improvement in the patient's dermatitis except for faint infraorbital erythema (Figure 2). The patient was advised to continue the tacrolimus ointment on an as-needed basis.

Comment

Topical steroids are paramount in treating many dermatologic diseases; however, their prolonged use has multiple side effects, most notably atrophy. Another side effect that may result from improper use is steroid-induced rosacea.

Several theories exist as to the pathogenesis of steroid-induced rosacea. Topical steroids may inhibit collagen synthesis, eventually causing dermal atrophy. The decrease in supporting connective tissue allows for passive dilation of the blood vessels and easier visualization of dermal capillaries, clinically resulting in prominent telangiectasias and background erythema.¹ Additionally, inflammatory papules and pustules may be caused by a reaction to increased colonization of pilosebaceous bacterial or fungal flora, though specific organisms have not been isolated yet.²

The rebound phenomenon of steroid-induced periocular dermatitis also is unclear. The vasoconstrictive action of corticosteroids may lead to the buildup of potent vasodilators such as nitric oxide. After the corticosteroid is discontinued, vessels dilate beyond their original diameter because of the accumulation of such vasodilators.³ Additionally, the immunosuppressive effect of corticosteroids may facilitate the overgrowth of microorganisms that may then act as superantigens. Withdrawal of immunosuppression may lead to an immunologic response and a heightened inflammatory reaction.⁴

Tacrolimus is a topical immunomodulator that mediates its effects through inhibition of calcineurin. Tacrolimus inhibits release of inflammatory

Accepted for publication March 27, 2003.

Drs. Pabby and Laws are from the Department of Dermatology and Skin Surgery, Roger Williams Medical Center, Providence, Rhode Island. Dr. An is from the Department of Internal Medicine, Rhode Island Hospital, Providence.

Reprints: Richard A. Laws, MD, Boston University School of Medicine, Department of Dermatology and Skin Surgery, Roger Williams Medical Center, Elmhurst Bldg, 50 Maude St, Providence, RI 08908 (e-mail: rlaws@earthlink.net).



Figure 1. A patient with periocular dermatitis resulting from approximately 12 months of topical steroid use. Note the erythematous papules on a background of erythema and few telangiectasias.



Figure 2. Minimal erythema at the infraorbital region of the face following a 3-week course of tacrolimus and oral tetracycline.

cytokines, most notably interleukin 2, and thus inhibits subsequent T-cell activation.⁵ Although tacrolimus and corticosteroids are comparable topical immunomodulators, they differ considerably in their side effect profile. Unlike topical corticosteroids, tacrolimus is minimally absorbed into the systemic circulation, does not accumulate in tissue, and does not cause decreased collagen synthesis and resultant atrophy. In addition, tacrolimus does not cause vasoconstriction and the subsequent rebound phenomenon seen with topical corticosteroid therapy. The most common side effects of tacrolimus are transient pruritus and burning on application.⁶

Tacrolimus recently has been approved by the US Food and Drug Administration for use in atopic dermatitis. A previous study of 3 patients with steroid-induced rosacea found that patients treated with tacrolimus ointment twice daily for 7 to 10 days experienced a mild rebound flare when the tacrolimus was discontinued. These patients subsequently had to be treated with oral doxycycline, topical clindamycin 1%, and sulfacetamide sodium 10% and sulfur 5% lotions for complete resolution.⁷ Our patient showed a rapid response and experienced no exacerbations of his periocular

rosacea with combination therapy of topical tacrolimus and oral tetracycline.

REFERENCES

1. Sibenge S, Gawkrödger DJ. Rosacea: a study of clinical patterns, blood flow, and the role of *Demodex folliculorum*. *J Am Acad Dermatol.* 1992;26:590-593.
2. Egan CA, Rallis TM, Meadows KP, et al. Rosacea induced by beclomethasone dipropionate nasal spray. *Int J Dermatol.* 1999;38:133-134.
3. Rapaport MJ, Rapaport V. Eyelid dermatitis to red face syndrome to cure: clinical experience in 100 cases. *J Am Acad Dermatol.* 1999;41:435-442.
4. Leung DYM. Atopic dermatitis: new insights and opportunities for therapeutic intervention. *J Allergy Clin Immunol.* 2000;105:860-876.
5. Ruzicka T, Assmann T, Homey B. Tacrolimus: the drug for the turn of the millennium? *Arch Dermatol.* 1999;135:574-580.
6. Berkery I, Fitzsimmons W, Tanase A, et al. Nonclinical and early clinical development of tacrolimus ointment for the treatment of atopic dermatitis. *J Am Acad Dermatol.* 2001;44(1 suppl):S17-S27.
7. Goldman D. Tacrolimus ointment for the treatment of steroid-induced rosacea: a preliminary report. *J Am Acad Dermatol.* 2001;44:995-998.