

Ethanol-Induced Flushing with Topical Pimecrolimus Use

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Topical calcineurin inhibitor use has been implicated in a flushing reaction associated with ethanol ingestion. This adverse effect has mostly been described as occurring with the application of tacrolimus ointment, and one report associated it with the use of pimecrolimus cream. We present three cases of ethanol-induced flushing in patients who used topical pimecrolimus.

Case 1

A 34-year-old man presented with a history of erythema and scaling on his scalp, face, chest, and back for several years, consistent with diagnoses of seborrheic dermatitis. He had previously been treated with topical ketoconazole, with marginal improvement; 1% pimecrolimus cream and topical ketoconazole were prescribed for the affected areas. The patient later reported flushing in the areas where he had applied the topical pimecrolimus 10 minutes after consuming beer. The flushing began to fade after 30 minutes and was completely clear in 2 hours. His history was negative for any prior known drug allergies or previous flushing with alcohol use. The flushing reaction with ethanol ingestion ended when topical pimecrolimus use was discontinued.

Case 2

A 46-year-old woman presented with erythematous papules and pustules on her face, consistent with the diagnosis of rosacea. After application of metronidazole gel failed to improve her condition, 1% pimecrolimus cream and minocycline were prescribed. The patient reported facial flushing after consuming beer once she began using 1% pimecrolimus cream regularly. Her history was negative for any prior known drug allergies or previous flushing with alcohol use. The flushing reaction with ethanol ingestion ended when the use of pimecrolimus cream was discontinued.

Case 3

A 29-year-old woman presented for evaluation of an itchy pink scaling eruption of her face, consistent with the diagnosis of seborrheic dermatitis. Among the treatments for this (prior to our evaluation) was topical pimecrolimus. This treatment led to flushing of the exposed areas immediately after alcohol ingestion. Her history was negative for any prior known drug allergies or previous flushing with alcohol use. The flushing reaction with ethanol ingestion ended when topical pimecrolimus cream was discontinued.

Discussion

Topical calcineurin inhibitor-associated alcohol intolerance has recently been described in the literature.¹ Tacrolimus has been linked most often with this flushing reaction in various case reports.^{2–5} This connection was also observed in a double-blind randomized trial in which 3.5% of patients treated with 0.3% tacrolimus ointment and 7% of patients treated with 0.1% tacrolimus ointment experienced this phenomenon, suggesting a dose-dependent relationship.⁶ Although it is a logical assumption that all topical medications in this class would elicit alcohol-induced flushing, there is only one report of this reaction occurring with 1% pimecrolimus cream.¹ This controlled observational study recorded moderate to severe flushing, limited to areas of topical pimecrolimus and tacrolimus application, just minutes following alcohol consumption.¹ In addition, the manufacturer of Elidel (Novartis, East Hanover, NJ) reports postmarketing incidents of skin flushing associated with alcohol use.⁷

The mechanism for this flushing reaction is unknown but has been postulated to be associated with aldehyde dehydrogenase inhibition at the site of topical calcineurin inhibitor application.¹ Prostaglandins may also mediate

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Reprints not available.

DOI 10.2310/6620.2008.07097

this reaction as aspirin has been reported to reduce the flushing effect.¹

Although tacrolimus has been coupled to this reaction, our report indicates that topical pimecrolimus is also associated with alcohol-induced flushing. Ensuring that patients are aware of and informed about this adverse effect may be warranted during treatment with topical pimecrolimus.

References

1. Ehst BD, Warshaw EM. Alcohol-induced application site erythema after topical immunomodulator use and its inhibition by aspirin [letter]. *Arch Dermatol* 2004;140:1014–5.
2. Calza A, Lubbe J. Tacrolimus ointment-associated alcohol intolerance in infants receiving ethanol-containing medication. *Br J Dermatol* 2005;152:569.
3. Knight AK, Boxer M, Chandler M. Alcohol-induced rash caused by topical tacrolimus. *Ann Allergy Asthma Immunol* 2005;95:291–2.
4. Lubbe J, Milingou M. Tacrolimus ointment, alcohol, and facial flushing. *N Engl J Med* 2004;351:2740.
5. Milingou M, Antille C, Sorg O, et al. Alcohol intolerance and facial flushing in patients treated with topical tacrolimus. *Arch Dermatol* 2004;140:1542–4.
6. Sotor N, Fleischer A, Webster G, et al. Tacrolimus ointment for the treatment of atopic dermatitis in adult patients: Part II, safety. *J Am Acad Dermatol* 2001;44:S39–46.
7. Novartis. Elidel. 2006. Available at: <http://www.pharma.us.novartis.com/product/pi/pdf/elidel.pdf> (accessed Dec 16, 2007).

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