Pimecrolimus and Tacrolimus for the Treatment of Intertriginous and Facial Psoriasis

Are They Effective?

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Commentary 1 on: Pimecrolimus cream 1% in the treatment of intertriginous psoriasis: a double-blind, randomized study.
Gribetz C, Ling M, Lebwohl M, et al

Question 1: What is the response of intertriginous psoriasis to topical pimecrolimus in comparison with vehicle?

Design: Randomized, participant- and outcome-evaluator-masked, vehicle-controlled trial.

Setting: Industry-sponsored, multicenter study of patients recruited from medical school and hospital departments of dermatology.

Patients: Adult patients with inverse psoriasis.

Intervention: Twice-daily application of 1% pimecrolimus cream or vehicle.

Main Outcome Measure: Percentage of patients reaching an investigator global assessment score of 0 (clear) or 1 (almost clear: mild erythema, no scaling, and no induration) by week 8 of treatment. A secondary outcome measure was the percentage of patients reaching a patient self-assessment score of 0 (complete disease control) or 1 (good disease control) by week 8 of treatment.

Results: At week 8, 20 (71%) of 28 and 6 (21%) of 29 patients treated with pimecrolimus and vehicle, respectively, achieved an investigator global assessment of 0 or 1 (difference in response rate, 0.51; number needed to treat [NNT], 2) (Table). At week 8, 23 (82%) of 28 and 12 (41%) of 29 patients treated with pimecrolimus and vehicle, respectively, achieved a patient self-assessment score of 0 or 1 (difference in response rate, 0.41; NNT, 3) (Table).

There were no serious adverse events, and no patient discontinued treatment because of adverse events. One patient treated with pimecrolimus developed paresthesia.

Authors’ Conclusions: One percent pimecrolimus cream is an effective treatment for inverse psoriasis with a rapid onset of actions and is safe and well tolerated.

Comment

This was a well-designed and well-executed study with clinically relevant and easy-to-understand primary and secondary outcomes. It supports the conclusion that pimecrolimus is effective for the treatment of intertriginous psoriasis. Its major limitation is its short duration and very small number of participants. With such limited numbers and short duration of therapy, no conclusions regarding safety can be drawn.

Commentary 2 on: Tacrolimus ointment is effective for facial and intertriginous psoriasis.
Lebwohl M, Freeman AK, Chapman MS, Feldman SR, Hartle JE, Henning A; Tacrolimus Ointment Study Group

Question 2: What is the response of intertriginous and facial psoriasis to topical tacrolimus ointment in comparison with vehicle?

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Outcome</th>
<th>Difference in Response Rate (95% CI)</th>
<th>NNT or NNH (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pimecrolimus</td>
<td>Clear or almost clear</td>
<td>0.51 (0.25 to 0.68)</td>
<td>2 (1.5 to 4)</td>
</tr>
<tr>
<td>Pimecrolimus</td>
<td>Patient-assessed complete or good disease control</td>
<td>0.41 (0.16 to 0.60)</td>
<td>3 (2 to 7)</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>Excellent improvement or clearing</td>
<td>0.30 (NP)</td>
<td>4 (NP)</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>Patient satisfied with effectiveness</td>
<td>0.42 (NP)</td>
<td>3 (NP)</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>Patient wished to continue treatment</td>
<td>0.37 (NP)</td>
<td>3 (NP)</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>Burning/stinging</td>
<td>0.01 (0.90 to 0.09)</td>
<td>132 (10 to 12)</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>Hyperesthesia</td>
<td>0.04 (0.03 to 0.10)</td>
<td>23 (34 to 10)</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>Itching</td>
<td>0.05 (0.03 to 0.12)</td>
<td>19 (34 to 9)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; NNH, number needed to harm; NNT, number needed to treat; NP, data not provided.
Design: Randomized, participant- and outcome-evaluator-masked, vehicle-controlled trial.
Setting: Industry-sponsored, randomized, multicenter study of patients recruited from academic medical center departments of dermatology.
Patients: Patients 16 years or older with facial or inverse psoriasis were randomized to treatment with 1% tacrolimus ointment or vehicle in a 2:1 allocation ratio.
Intervention: Twice-daily application of 1% tacrolimus ointment or vehicle.
Main Outcome Measures: Percentage of patients reaching a physician’s global assessment of clear (100% improvement) or excellent improvement (90% to 99% improvement) by week 8 of treatment. Patient satisfaction was evaluated using a Likert scale that ranked the patient’s level of agreement with 5 statements.
Results: At week 8, 67% and 37% of patients treated with 1% tacrolimus ointment and vehicle, respectively, achieved a physician’s global assessment of clear or excellent improvement (difference in response rate, 0.30; NNT, 4) (Table). At week 8, 63% and 21% of patients treated with 1% tacrolimus ointment and vehicle, respectively, were satisfied with effectiveness (difference in response rate, 0.42; NNT, 3). At 8 weeks, 58% and 21% of patients treated with 1% tacrolimus ointment and vehicle, respectively, wished to continue treatment (difference in response rate, 0.37; NNT, 3) (Table).
At week 8, 5 (5%) of 112 and 0 (0%) of 55 patients treated with 1% tacrolimus ointment and vehicle, respectively, had hyperesthesia (difference in complication rate, 0.04; number needed to harm, 23) and 8 (7%) of 112 and 1 (2%) of 55 patients treated with 1% tacrolimus ointment and vehicle, respectively, had itching (difference in complication rate, 0.05; number needed to harm, 19) (Table).

Authors’ Conclusion: Tacrolimus ointment is an effective treatment for psoriasis of the face or intertriginous areas.

Comment

The design and reporting limitations of the study limit the ability to draw firm conclusions regarding efficacy. Because the percentages of patients having facial psoriasis vs intertriginous psoriasis are not reported separately, and the results in the 2 conditions are also combined, it is impossible to relate findings to people with intertriginous or facial psoriasis. The physician’s global assessment is not defined enough to be clinically interpretable. Actual numbers of responders and confidence intervals are not provided and could not be calculated from the data provided. The article would have been more useful to the reader if it were more compliant to the following principles of the CONSORT statement that ensures high-quality reporting of randomized controlled trials:

1. State the point estimate (treatment effect) and its precision (confidence interval).
2. State results in absolute numbers (eg, 10/20, not 50%).
3. Present data in sufficient detail to permit alternative analyses.
4. Describe prognostic variables by treatment group (eg, actual numbers and responders with facial or intertriginous psoriasis).

Author’s Conclusion: Tacrolimus ointment is an effective treatment for intertriginous and facial psoriasis, but come with a concern that atrophy of the skin and rosacea may develop with long-term facial use. Studies to determine topical corticosteroid dosing schedules that are effective and do not produce atrophy or rosacea are limited. An effective treatment for facial and intertriginous psoriasis without the fear of producing atrophy would be a welcome addition to dermatologists’ therapeutic armamentarium. Previous studies of pimecrolimus cream and tacrolimus ointment have been limited to small, uncontrolled trials and case series. Pimecrolimus appears to be an effective treatment for intertriginous psoriasis in this small 8-week study. Its safety and long-term efficacy can only be determined by further study. The tacrolimus study needs to be more completely reported or further studied before we can draw firm conclusions regarding efficacy or safety.

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