Response of Oral Lichen Planus to Topical Tacrolimus in 37 Patients

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Background: Topical tacrolimus has been reported to be effective for the treatment of oral lichen planus. This article describes our experience with topical tacrolimus in patients treated for symptomatic oral lichen planus.

Observations: A survey was mailed to 40 patients with symptomatic oral lichen planus treated with topical tacrolimus. Surveys were completed by 37 patients (93%) a mean of 1.3 years after initiation of treatment. Thirty-three (89%) of the 37 patients reported symptomatic improvement, and 31 (84%) reported partial to complete lesion clearance while using topical tacrolimus. On average, patients noted improvement in 1 month. Twelve patients (32%) reported adverse effects consistent with those reported previously (ie, burning, irritation, and tingling). Among the 28 patients still using the medication, 15 patients (54%) apply it at least once daily. Of the 9 patients who discontinued using the medication, 5 experienced recurrence.

Conclusions: Topical tacrolimus is effective for the treatment of oral lichen planus. Most patients experienced symptomatic improvement in less than 1 month. However, the effect is temporary; when topical tacrolimus is discontinued, oral lichen planus may flare again.

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deposition of fibrinogen along the basement membrane zone27,28); (2) symptoms of pain, irritation, or both; and (3) prescription and use of topical tacrolimus.

Patients who responded that their symptoms were somewhat better or much better were considered to have symptomatic improvement. Response was defined as reports that better or much better were considered to have symptomatic improvement. Response was defined as reports that better or much better were considered to have symptomatic improvement.

Forty patients with symptomatic OLP who had been prescribed topical tacrolimus (twice-daily applications to the affected areas) were mailed a survey. Thirty-nine (98%) of the 40 patients responded that they were using the medication, and 1 patient responded that he did not fill the prescription. Two patients wrote a comment on the survey and did not complete the questionnaire. One responded that topical tacrolimus made her tongue feel as if it had been burned, and the other responded that he had difficulty getting the medication to stay on his cheeks. Our results are from the remaining 37 patients (93%) who used the medication and responded to the survey.

Because the commercial form of topical tacrolimus was not yet available, some patients were initially prescribed a formulation of tacrolimus mixed with a petrolatum ointment (Aquaphor; Beiersdorf, South Norwalk, Conn) to make 0.03% and 0.1% concentrations. Fourteen patients (38%) initially received the 0.03% concentration and 1 patient (2%) the 0.1% concentration in petrolatum, but the commercial product was prescribed for all patients when it became available. Twenty-two patients were initially prescribed commercially prepared topical tacrolimus, 18 patients (49%) the 0.03% concentration, and 4 patients (11%) the 0.1% concentration.

Patient demographics and clinical characteristics are summarized in Table 2. The mean age of the 32 women and 3 men was 64 years (range, 38-82 years). Twenty-three (62%) of the 37 patients had predominantly reticulated lichen planus, and 14 (38%) had predominantly erosive lichen planus. All patients had OLP, some at more than 1 site. Concomitant genital involvement was present in 11 patients (30%) and cutaneous involvement in 3 patients (8%). Two (5%) had oral involvement, and 1 (3%) had esophageal lichen planus. Twenty-five patients (68%) had histopathologic confirmation of lichen planus, and 11 (30%) had supportive results from direct immunofluorescence studies.

The mean duration of OLP before starting topical tacrolimus treatment was 4.4 years. Prior treatment had been unsuccessful in nearly all patients (35 of 37). In the 2 remaining patients, topical tacrolimus was first-line therapy. One patient continues to take hydroxychloroquine, 1 patient continues to take oral corticosteroids, and 3 patients continue to use topical antifungals intermittently.

The responses to the survey are summarized in Table 3. Surveys were completed a mean of 1.3 years after initiation of topical tacrolimus treatment (range, 49 days to 2.7 years). Thirty-one patients (84%) reported

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**Table 1. Review of Studies of Symptomatic Oral Lichen Planus (OLP) Treated With Topical Tacrolimus**

<table>
<thead>
<tr>
<th>Source</th>
<th>No. of Biopsy-proven OLP Cases</th>
<th>Type of Tacrolimus Used</th>
<th>Degree of Lesion Response, No.</th>
<th>Time to Response</th>
<th>Follow-up Time</th>
<th>Time to Lesion Relapse After Stopping Treatment, No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vente et al21</td>
<td>4</td>
<td>0.1% in petrolatum</td>
<td>Complete resolution, 3; improved, 1</td>
<td>4 wk</td>
<td>7-16 wk</td>
<td>Within 3-8 wk, 4</td>
</tr>
<tr>
<td>Rozycki et al22</td>
<td>12</td>
<td>0.03%, 0.1%, and 0.3% in petrolatum</td>
<td>Responded, 11; did not respond, 2</td>
<td>In 5 patients, 1 mo</td>
<td>1-12 mo (mean, 6.5 mo)</td>
<td>Within 1-2 wk, 4</td>
</tr>
<tr>
<td>Kaliakatsou et al24</td>
<td>19</td>
<td>0.1% in paraffin ointment</td>
<td>Responded, 17</td>
<td>Some response, 1 wk; complete response, 1 mo</td>
<td>22 wk</td>
<td>Within 2-15 wk, 13 (mean, 4 wk)</td>
</tr>
<tr>
<td>Lener et al22</td>
<td>1</td>
<td>0.1% in petrolatum,</td>
<td>Responded</td>
<td>Lip, 1 mo; intraoral, 3 mo</td>
<td>12 mo</td>
<td>No relapse at 1 y</td>
</tr>
<tr>
<td>Olivier et al26</td>
<td>8</td>
<td>Mouthwash tacrolimus</td>
<td>Improved, 7; no response, 1</td>
<td>In 7 patients, 1 mo</td>
<td>12 mo</td>
<td>Within 12 mo, 7</td>
</tr>
<tr>
<td>Morrison et al25</td>
<td>Unknown</td>
<td>0.1% in petrolatum</td>
<td>Improved, 6</td>
<td>Some response, 2 wk; complete response in all patients, 1 mo</td>
<td>3 mo</td>
<td>Within 2 wk, 2</td>
</tr>
</tbody>
</table>

**RESULTS**
that they were somewhat or very satisfied with topical tacrolimus treatment and that they would recommend the medication to others.

On average, patients used topical tacrolimus for 1.1 years (range, 5 days to 2.7 years) and reported an improvement within 1 month (range, 3 days to 6 months). Thirty-four patients (92%) reported that they used the medication as instructed all the time or most of the time. Symptomatic improvement was reported by 33 patients (89%). Thirty-one patients (84%) reported partial to complete lesion clearance with topical tacrolimus treatment (Figure). One patient reported that the lesions increased, and 1 reported that the symptoms were much worse.

Clinical findings after topical tacrolimus use were available for 24 of the 37 patients. Of these 24 patients, 5 did not have a follow-up visit until 1 year or more after starting topical tacrolimus treatment because of traveling constraints; of these 5 patients, 2 had clinical improvement and 3 had resolution of their OLP lesions. The remaining 19 patients were seen a mean of 2 months after initiation of topical tacrolimus treatment; of these, 12 had clinical improvement and 7 had resolution of their OLP lesions.

Twenty-five patients (68%) reported no difficulties, and 12 patients (32%) reported experiencing problems with using the medication. Of these 12 patients, 4 (11%) reported that the medicine caused irritation; 5 (14%), that it caused burning; and 3 (8%), that it caused tingling. Two patients (17%) also reported an objectionable taste. Four patients each reported other problems: bad breath, extra phlegm in the mouth, swelling of the mouth and lips, and teeth problems.

Twenty-eight patients (76%) continue to use topical tacrolimus. The mean follow-up of the patients still using topical tacrolimus is 1.3 years (range, 49-968 days). Fifteen (54%) of these 28 patients apply the medication more than once daily. The remaining 13 patients use topical tacrolimus twice weekly or less.

Of the 9 patients (24%) not currently using topical tacrolimus, 5 reported that they discontinued the medication because of adverse effects, 1 because she did not notice any change in the lichen planus, and 2 because the lichen planus was better. These patients applied the medi-
cation for an average of 4.9 months (range, 5 days to 1.3 years). After stopping treatment with topical tacrolimus, 5 patients (56%) reported that the lichen planus returned, and 3 (33%) reported that it stayed the same. The remaining patient did not answer this question.

**COMMENT**

Topical tacrolimus treatment was safe and effective in most patients, 89% of whom experienced symptomatic response and 84% of whom reported lesion clearance. Lesions responded to treatment within 6 months (mean, 1 month).

The demographic characteristics of our patients were similar to those of patients previously reported. Our patients had both erosive and reticulated OLP, whereas most prior reports focused on erosive OLP alone. Treatment with topical tacrolimus appears to be effective for both erosive and reticulated forms of OLP.

Also, 30% of our patients had genital involvement associated with OLP, and 8% had either otic or esophageal involvement. It has been reported that patients with OLP associated with genital lichen planus (the vulvovaginal gingival syndrome) typically are more difficult to treat than those with other forms of lichen planus.1-6 All 11 patients with both oral and genital lesions had symptomatic improvement in both areas. These data are discussed further in another article.29 The 2 patients with otic involvement also had improvement in their otic lichen planus with a topical tacrolimus suspension.

Topical tacrolimus treatment was effective as first-line therapy in 2 patients. Thirty-one patients whose OLP was recalcitrant to other therapies reported topical tacrolimus to be effective. Two patients who responded to the questionnaire continued systemic treatment, one with hydroxychloroquine and the other with corticosteroids; in both patients, OLP improved markedly with the addition of topical tacrolimus. Symptoms were unchanged in 3 patients, and 1 patient reported that symptoms and lesions worsened while using topical tacrolimus.

Adverse effects were reported by one third of patients, and they were similar to those previously reported (irritation, burning, and/or tingling). Only 5 patients discontinued use of topical tacrolimus because of adverse effects; in the remaining patients, adverse effects resolved with continued use.

Most of our patients continue to use topical tacrolimus. Although topical tacrolimus is effective at controlling disease, we found that it rarely seems to result in complete remission of OLP. This is consistent with observations from prior studies.21-26 Long-term use (>1 year) did not result in any serious adverse effects in our patients, most of whom were satisfied with topical tacrolimus treatment.

This is a retrospective study with a patient survey and therefore is subject to patient recall bias. However, the mailed survey was the most effective way to follow up with our patients, who often live a great distance from our clinic. The survey offered a standardized, objective way to obtain our data, and the patients who were able to return for follow-up had clinical findings that correlated with the survey results.

In summary, we followed up 37 patients with symptomatic OLP by means of a mailed questionnaire. Most of these patients responded to topical tacrolimus treatment with both clinical and symptomatic improvement. The effect of topical tacrolimus usually occurred within 1 month of treatment; however, most patients require maintenance therapy. No serious adverse effects of topical tacrolimus were noted after more than 1 year of follow-up, which supports the thesis that topical tacrolimus is a safe and effective treatment for OLP.

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**REFERENCES**


A variety of adverse cutaneous reactions have been described, ranging from self-limiting dermatitic rashes to erythroderma for which cessation of therapy was required. Also reported were reactions similar to graft-vs-host disease, erythema nodosum, small-vessel vasculitis, exanthematous pustulosis, and Stevens-Johnson syndrome. Sweet syndrome has been associated with chronic myeloid leukemia, but the association is rare, and the only times our patient developed skin lesions were after the administration of imatinib.

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REFERENCES


Correction

Error in the Figure: In the article by Byrd et al titled “Response of Oral Lichen Planus to Topical Tacrolimus in 37 Patients” published in the December 2004 issue of the ARCHIVES (2004;140:1508-1512), parts A and B in the Figure were transposed. We regret the error.