

## Review Article

## MANAGEMENT OF ORAL LICHEN PLANUS

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Oral lichen planus (OLP) is a chronic inflammatory disease characterized by relapses and remissions. There is currently no cure for OLP. Treatment is aimed primarily at reducing the length and severity of symptomatic outbreaks. Topical steroids are the first-choice agent for the treatment of symptomatic, active OLP. Other topical agents that have been used in cases resistant to topical steroids include retinoids, cyclosporine, and tacrolimus. Oral and topical psoralen with a low dose of UVA is effective in treating OLP of various forms, but it seems to have too many side effects. Topical application of psoralen is promising, but is still at experimental stage.

The treatment of symptomatic OLP, especially the erosive variant, represents a perplexing therapeutic challenge. Despite numerous existing remedies, there are many treatment failures.

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## Introduction

Lichen planus is an inflammatory disease that involves skin and mucosa. It is one of the most common oral diseases that manifests itself in the oral cavity.<sup>1</sup> The exact cause is unknown, but the immunologic system plays a leading role in the pathogenesis.<sup>2</sup> It is well documented that oral lichen planus (OLP) represents a cell-mediated immune response with infiltrating cell population composed of both T4 and T8 lymphocytes.<sup>3</sup>

OLP is mainly seen in women and characteristically the lesions are symmetrical, involving the buccal mucosa, tongue, gingiva, floor of the mouth, lips, and palate.<sup>4</sup>

The differential diagnosis of OLP, presenting as white patches or hyperkeratotic striae, is broad and includes lichenoid lesions, leukoplakia, lupus erythematosus, chronic ulcerative stomatitis, and rarely malignancy. In some patients, however, oral lesion presents as desquamative gingivitis.

Up to now different therapies are described for OLP including drug therapy, surgery, psoralen

with ultraviolet light A (PUVA), and laser. In this article, these methods would be reviewed.

## Drug therapy

Drug therapy is the most common method for treatment of OLP. Different drugs have been used for treatment of OLP including immunosuppressives, retinoids, and immunomodulators. Drugs are used in two forms, topical or/and systemic.

## Topical drug therapy

Topical drug therapy is a method of treatment in which drugs are applied directly to the part being treated (e.g., skin, eyes, or mucosa). Various kinds of drugs are used in topical form for treatment of OLP including corticosteroids, immunosuppressives, retinoids, and immunomodulators.

## Topical steroid therapy

High-potency topical corticosteroids in an adhesive medium appear to be the safest and most effective treatment of OLP.<sup>5-7</sup> For topical applications, we usually use them as gel, oral paste, or solution. Triamcinolone has been tried for the treatment of OLP. A number of investigations have determined the efficacy of triamcinolone acetonide 0.1% suspension in the treatment of

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OLP. This drug is available over the counter and is useful in the treatment of OLP.<sup>8</sup>

Fluocinolone is another steroid, which has been used for treatment of OLP. Compared with the placebo, this drug has been found to be more effective.<sup>7</sup> A study evaluated fluocinolone acetonide 0.1% in three groups: solution (FAS), Orabase (FAO), and both. The best results achieved with FAO. This study had a long-term follow-up, without having a control group.<sup>9</sup> Another study used fluocinolone acetonide gel 0.1% and fluocinolone acetonide 0.1% in Orabase. There was no significant difference between the 2 groups. This study did not have any control group either, and was in the form of a short follow-up.<sup>10</sup> A study confirmed the efficacy of topical fluocinolone acetonide gel 0.025 %, along with the topical antimicrobial drug chlorhexidine, in treatment of erosive OLP.<sup>11</sup>

Clobetasol has been studied too. Clobetasol propionate 0.05% ointment has been shown to heal OLP, but this study had a small sample group, without any control group or follow-up.<sup>12</sup> Among the three preparations of clobetasol propionate 0.05% (ointment, Orabase, and the adhesive denture paste) the best results have been achieved with clobetasol propionate in an adhesive denture paste. However, there were no long-term follow-up and control group.<sup>5</sup>

Relative efficacy of fluocinolone acetonide 0.1% had been compared with triamcinolone acetonide 0.1%. The results showed that fluocinolone acetonide is more effective in the majority of cases.<sup>13</sup>

Another study showed no difference between the fluticasone propionate (FP) spray and betamethasone sodium phosphate (BSP) mouth rinse. But FP was found to be more acceptable to patients than BSP, because of the convenience of the spray form.<sup>14</sup>

### Topical retinoid therapy

Retinoids are metabolites of vitamin A. They have been noted to have antikeratinizing and immunomodulating effects.<sup>3, 15, 16</sup> The efficacy of these drugs has been assessed in several studies. In two studies, retinoids were successfully used to treat OLP in cases where corticosteroids failed to achieve satisfactory results.<sup>17</sup>

Retinaldehyde 0.1% was assessed in the treatment of OLP and leukoplakia. This drug showed good clinical efficacy, but there was no long-term follow-up and any control group.<sup>17</sup>

Isotretinoin gel 0.1% has also been suggested as an alternative to topical corticosteroids in the management of OLP.<sup>18</sup>

OLP has been treated with fenretinide and tazarotene gel 0.1% successfully.<sup>19, 20</sup> These studies suggested that topical retinoid might be a suitable therapeutic agent in the treatment of hyperkeratotic OLP, but they had no long-term follow-ups. The efficacy of retinoic acid in Orabase (0.05%) has been compared with fluocinolone acetonide in Orabase (0.1%), on atrophic and erosive OLP. The results suggested that fluocinolone acetonide 0.1% reduced the severity of OLP better than retinoic acid 0.05%.<sup>3</sup> Also, the efficacy of retinoic acid 0.05% has been compared with triamcinolone acetonide 0.1%, both in Orabase. The results showed that in nonkeratotic and even keratotic OLP, topical triamcinolone acetonide 0.1% reduced the severity of lesions more effectively than topical retinoic acid 0.05%.<sup>21</sup>

### Topical immunosuppressive drug therapy

Immunosuppressives are a large group of drugs which are used in the treatment of immunological diseases such as OLP.

Topical cyclosporine A (CSA) has been assessed by some investigators. In a study, topical CSA was used on a small sample group and results showed its benefits in the treatment of OLP.<sup>22</sup> Some other studies have used different doses of CSA and reported CSA as an effective agent for OLP.<sup>23 – 25</sup> The most localized side effect of CSA is a transient burning sensation. However, several studies have not found any efficacy for CSA.<sup>26, 27</sup> A study suggested that CSA could be used as an alternative agent for the conventional treatment of acute periods of OLP, but it can't be considered as a first choice because of its cost.<sup>28</sup>

Tacrolimus and pimecrolimus are usually used after transplantation. The results of some studies suggested a rapid and important palliating effect of low concentration of topical tacrolimus and pimecrolimus, but no large clinical trials have been conducted and long-term follow-ups have found relapse of the disease.<sup>29 – 33</sup>

### Analgesics

For symptomatic therapy, the use of a variety of topical analgesics is recommended. Diphenhydramine elixir as mouthwash and xylocaine gel can be safely used along side other therapeutic agents.<sup>34</sup>

### Systemic drug therapy

In this method, drugs affect the body as whole rather than individual parts and organs. When the use of topical drugs alone has failed to achieve an adequate control, clinicians use systemic agents. Corticosteroids are usable, but there are not enough double-blind, controlled clinical trials, evaluating the efficacy of systemic corticosteroids in the management of OLP. Nevertheless, prednisolone may be of value in the management of acute episodes (30 – 60 mg daily for 2 – 3 weeks).<sup>34</sup>

Systemic retinoids have severe side effects, so nowadays they are not used for the treatment of OLP. However, there has been one controlled trial, comparing etretinate with placebo. In these patients, a prompt improvement was noted compared with the control group. Also, the relapse rate was high (about 60%) after 3 months.<sup>35</sup>

Other drugs which are used systemically are thalidomide,<sup>36, 37</sup> metronidazole,<sup>38</sup> griseofulvin,<sup>39</sup> and hydroxychloroquine.<sup>40</sup> The immunomodulatory activity of these drugs seems to be a possible mechanism of action beside their antimicrobial activity, but there is not much clinical trails for them.

### Surgery

Surgical excision, cryotherapy, CO<sub>2</sub> laser, and ND:YAG laser have all been used in the treatment of OLP. In general, surgery is reserved to remove high-risk dysplastic areas.<sup>34</sup>

### Laser

The 308 nm excimer laser has been used as a possible and additional method in the treatment of OLP. Treatments are painless and well tolerated. Clinical improvement has been achieved in most patients. Excimer 308 nm lasers could be an effective choice in treating symptomatic OLP.<sup>41 – 43</sup>

### Photochemotherapy

In this method, clinician uses ultraviolet A (UVA) with wavelengths ranging from the 320 – 400 nm, after the injection of psoralen.

The use of PUVA therapy in OLP waits further evaluation in large controlled trails. In two studies, UVA was applied to lesions, 2 hours after the injection of psoralen. After 2 months, most of the lesions had been notably improved and the remission times ranged from 2 to 17 months.<sup>44, 45</sup>

One potential draw back of PUVA therapy is the risk of the squamous cell carcinoma (SCC)

development in a condition with premalignant potential, and until more extensive studies have been performed, it must be considered as an experimental method.<sup>44, 45</sup>

### Conclusion

No treatment has demonstrated convincingly its superiority over topical corticosteroid, the acceptable first-line choice mentioned in most reviews.<sup>46 – 50</sup> The second-line therapy in plaque-like LP should be topical retinoids, but a strong evidence for efficacy is lacking. All other agents are unapproved treatments, with uncertain or doubtful efficacy. The use of topical cyclosporine A could be recommended as third-line therapy in severe multiple drug-resistant cases.<sup>44</sup>

### References

- 1 Silverman JR, Bahl S. Oral lichen planus update: clinical characteristics. Treatment, responses, and malignant transformation. *Am J Dent.* 1997; **10**: 259 – 263.
- 2 Gorky M, Raviv M, Moskona D, et al. Clinical chemical characteristic and treatment of patients with oral lichen planus in Israel. *Oral Surg Oral Med Oral Pathol.* 1996; **82**: 644 – 649.
- 3 Buajeeb W, Kraivaohan P, Poburksa C, et al. Efficacy of topical retinoic acid compared with topical fluocinolone acetonide in the treatment of oral lichen planus. *Oral Surg Med Oral Pathol.* 1997; **83**: 21 – 25.
- 4 Jungell P, Malmstrom M. Cyclosporine A mouthwash in the treatment of oral lichen planus. *Int J Oral Maxillofac Surg.* 1996; **25**: 60 – 62.
- 5 Lomuzio L, Dellavalle A, Mignogna M, et al. The treatment of oral aphthous ulceration of erosive lichen planus with topical clobetasol propionate in three preparations: a clinical and pilot study on 54 patients. *J Oral Pathol Med.* 2001; **30**: 64 – 67.
- 6 Plemmons J, Ree T, Zachariah N. Absorption of topical steroid and evaluation of adrenal suppression in patients with erosive lichen planus. *Oral Surg Oral Med Oral Pathol.* 1990; **69**: 42 – 44.
- 7 Voute AB, Schulten EA, Langendijk PN, Kostense PJ, van der Waal I. Fluocinolone in an adhesive base for treatment of oral lichen planus. A double-blind, placebo-controlled clinical study. *Oral Surg Oral Med Oral Pathol;* 1993; **75**: 181 – 185.
- 8 Rabiyl M, Sahebamee M. Effect of aqueous triamcinolone actonide 0.2% suspension in treatment of oral lichen planus. *Journal Medical Faculty Guilan University of Medical Sciences.* 2003; **12**: 6 – 14.
- 9 Thongprasom K, Luengvisut P, Wongwatanakij A, Boonjatturus C. Clinical evaluation in treatment of oral lichen planus with topical fluocinolone acetonide: a 2-year follow-up. *J Oral Pathol Med.* 2003; **32**: 315 – 322.
- 10 Buajeeb W, Poburksa C, Kraivaphan P. Efficacy of fluocinolone acetonide gel in the treatment of oral lichen planus. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2000; **89**: 42 – 45.
- 11 Carbone M, Carrozzo M, Broccoletti R, Mattea A, Gandolfo S. The topical treatment of atrophic-erosive

- oral lichen planus with fluocinolone in a bioadhesive gel, chlorhexidine, and miconazole gel. A totally open trial [Italian]. *Minerva Stomatol.* 1996; **45**: 61 – 68.
- 12 Roed-Petersen B, Roed-Petersen J. Occlusive treatment of atrophic and erosive oral lichen planus with clobetasol propionate 0.05% ointment (Dermovat) [Danish]. *Tandlaegernes Tidsskr.* 1992; **1**: 4 – 7.
  - 13 Thongprasom K, Luangjarmekorn L, Sererat T, Taweessap W. Relative efficacy of fluocinolone acetonide compared with triamcinolone acetonide in treatment of oral lichen planus. *J Oral Pathol Med.* 1992; **21**: 456 – 458.
  - 14 Hegarty AM, Hodgson TA, Lewsey JD, Porter SR. Fluticasone propionate spray and betamethasone sodium phosphate mouthrinse: a randomized crossover study for the treatment of symptomatic oral lichen planus. *J Am Acad Dermatol.* 2002; **47**: 271 – 279.
  - 15 Pawson BA, Ehmman CW, Itri LM, Sherman MI. Retinoids at the threshold: their biological significance and therapeutic potential. *J Med Chem.* 1982; **25**: 1269 – 1277.
  - 16 Voorhees JJ, Orfanos CE. Oral retinoids. Broad-spectrum dermatologic therapy for the 1980s. *Arch Dermatol.* 1981; **117**: 418 – 421.
  - 17 Becker LE, Bergstresser PR, Whiting DA, et al. Topical clindamycin therapy for acne vulgaris. A cooperative clinical study. *Arch Dermatol.* 1981; **117**: 482 – 485.
  - 18 Giustina TA, Stewart JC, Ellis CN, et al. Topical application of isotretinoin gel improves oral lichen planus. A double-blind study. *Arch Dermatol.* 1986; **122**: 534 – 536.
  - 19 Tradati N, Chiesa F, Rossi N, et al. Successful topical treatment of oral lichen planus and leukoplakias with fenretinide (4-HPR). *Cancer Lett.* 1994; **76**: 109 – 111.
  - 20 Petrucci M, De Benedittis M, Grassi R, Cassano N, Vena G, Serpico R. Oral lichen planus: a preliminary clinical study on treatment with tazarotene. *Oral Dis.* 2002; **8**: 291 – 295.
  - 21 Sahebjamiee M, Amanolu M, Bakhshi M. Efficacy of topical retinoic acid compared with topical triamcinolone acetonide in the treatment of oral lichen planus. *Acta Medica Iranica.* 2004; **42**: 108 – 113.
  - 22 Itin P, Surber C, Buchner S. Lack of effect after local treatment with a new cyclosporine formulation in recalcitrant erosive oral lichen planus. *Dermatology.* 1992; **185**: 262 – 265.
  - 23 Eisen D, Ellis CN, Duell EA, Griffiths CE, Voorhees JJ. Effect of topical cyclosporine rinse on oral lichen planus. A double-blind analysis. *N Engl J Med.* 1990; **323**: 290 – 294.
  - 24 Eisen D, Griffiths CE, Ellis CN, Nickoloff BJ, Voorhees JJ. Cyclosporine washes for oral lichen planus. *Lancet.* 1990; **335**: 535 – 553.
  - 25 Porter SR, Scully C, Eveson JW. The efficacy of topical cyclosporine in the management of desquamative gingivitis due to lichen planus. *Br J Dermatol.* 1993; **129**: 753 – 755.
  - 26 Ho VC, Conklin RJ. Effect of topical cyclosporine rinse on oral lichen planus. *N Engl J Med.* 1991; **325**: 435.
  - 27 Levell NJ, MacLeod RI, Marks JM. Lack of effect of cyclosporine mouthwash in oral lichen planus. *Lancet.* 1991; **337**: 796 – 797.
  - 28 Lopez-Lopez J, Rosello-Llabres X. Cyclosporine A, an alternative to the oral lichen planus erosive treatment. *Bull Group Int Rech Sci Stomatol Odontol.* 1995; **38**: 33 – 38.
  - 29 Esquivel-Pedraza L, Fernandez-Cuevas L, Ortiz-Pedroza G, Reyes-Gutierrez E, Orozco-Topete R. Treatment of oral lichen planus with topical pimecrolimus 1% cream. *Br J Dermatol.* 2004; **150**: 771 – 773.
  - 30 Byrd JA, Davis MD, Bruce AJ, Drage LA, Rogers RS 3rd. Response of oral lichen planus to topical tacrolimus in 37 patients. *Arch Dermatol.* 2004 Dec; **140**: 1508 – 1512. Erratum in: *Arch Dermatol.* 2005 Mar; **141**: 370.
  - 31 Thomson MA, Hamburger J, Stewart DG, Lewis HM. Treatment of erosive oral lichen planus with topical tacrolimus. *J Dermatolog Treat.* 2004; **15**: 308 – 314.
  - 32 Dissemond J, Schroter S, Franckson T, Herbig S, Goos M. Pimecrolimus in an adhesive ointment as a new treatment option for oral lichen planus. *Br J Dermatol.* 2004; **150**: 782 – 784.
  - 33 Hodgson TA, Sahni N, Kaliakatsou F, Buchanan JA, Porter SR. Long-term efficacy and safety of topical tacrolimus in the management of ulcerative/erosive oral lichen planus. *Eur J Dermatol.* 2003; **13**: 466 – 470.
  - 34 Setterfield JF, Black MM, Challacombe SJ. The management of oral lichen planus. *Clin Exp Dermatol.* 2000; **25**: 176 – 182.
  - 35 Hersle K, Mobacken H, Sloberek-Thilander H. Severe oral lichen planus treatment with an aromatic retinoid (etretinate). *Br J Dermatol.* 1982; **106**: 77 – 80.
  - 36 Camisa C, Popovsky JL. Effective treatment of oral erosive lichen planus with thalidomide. *Arch Dermatol.* 2000; **136**: 1442 – 1443.
  - 37 Macario-Barrel A, Balguerie X, Joly P. Treatment of erosive oral lichen planus with thalidomide [French]. *Ann Dermatol Venerol.* 2003; **130**: 1109 – 1112.
  - 38 Buyuk AY, Kavala M. Oral metronidazole treatment of lichen planus. *J Am Acad Dermatol.* 2000; **43**: 260 – 262.
  - 39 Matthews RW, Scully C. Griseofulvin in the treatment of oral lichen planus: adverse drug reactions, but little beneficial effect. *Ann Dent.* 1992; **51**: 10 – 11.
  - 40 Eisen D. Hydroxychloroquine sulfate (Plaquenil) improves oral lichen planus: an open trial. *J Am Acad Dermatol.* 1993; **28**: 609 – 612.
  - 41 Kollner K, Wimmershoff M, Landthaler M, Hohenleutner U. Treatment of oral lichen planus with the 308-nm UVB excimer laser—early preliminary results in eight patients. *Lasers Surg Med.* 2003; **33**: 158 – 160.
  - 42 Passeron T, Zakaria W, Ostovari N, Mantoux F, Lacour JP, Ortonne JP. Treatment of erosive oral lichen planus by the 308 nm excimer laser. *Lasers Surg Med.* 2004; **34**: 205.
  - 43 Trehan M, Taylor CR. Low-dose excimer 308-nm laser for the treatment of oral lichen planus. *Arch Dermatol.* 2004; **140**: 415 – 420.
  - 44 Lehtinen R, Happonen RP, Kuusilehto A, Jansen C. A clinical trial of PUVA treatment in oral lichen planus. *Proc Finn Dent Soc.* 1989; **85**: 29 – 33.
  - 45 Lundquist G, Forsgren H, Gajecki M, Emtestam L. Phototherapy of oral lichen planus. A controlled study. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 1995; **79**: 554 – 558.
  - 46 Cribier B, Frances C, Chosidow O. Treatment of lichen planus. An evidence-based medicine analysis of efficacy. *Arch Dermatol.* 1998; **134**: 1521 – 1530.
  - 47 Zegarelli DJ. Multimodality steroid therapy of erosive and ulcerative oral lichen planus. *J Oral Med.* 1983;

- 38:**127 – 130.
- 48** Eisen D. The therapy of oral lichen planus. *Crit Rev Oral Biol Med.* 1993; **4:** 141 – 158.
- 49** No authors listed. Treatment of oral lichen planus. Lancet. 1990; **336:** 913 – 914.
- 50** Gribier B, Chosidow O. Lichen. *Ann Dermatol Venereol.* 1997; **124:** 61 – 68.