MANAGEMENT OF ORAL LICHEN PLANUS

Mahnaz Sahebjamee DMD\*, Fatemeh Arbabi-Kalati DMD

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 it 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.

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.\(^1\) The exact cause is unknown, but the immunologic system plays a leading role in the pathogenesis.\(^2\) 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.\(^3\)

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.\(^4\)

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.\(^5\) - \(^7\) 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...
OLP. This drug is available over the counter and is useful in the treatment of OLP.8

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.7 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.9 Another study used fluocinolone acetonide gel 0.1% and fluocinolone acetonide 0.1% in Orabase. There was no significant difference between the two groups. This study did not have any control group either, and was in the form of a short follow-up.10 A study confirmed the efficacy of topical fluocinolone acetonide gel 0.025 %, along with the topical antimicrobial drug chlorhexidine, in the treatment of erosive OLP.11

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.12 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.5

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.13

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.14

Topical retinoid therapy

Retinoids are metabolites of vitamin A. They have been noted to have antikeratinizing and immunomodulating effects.3, 15, 16 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.17

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.17 Isotretinoin gel 0.1% has also been suggested as an alternative to topical corticosteroids in the management of OLP.16

OLP has been treated with fenretinide and tazarotene gel 0.1% successfully.19, 20 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%.3 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%.21

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.22 Some other studies have used different doses of CSA and reported CSA as an effective agent for OLP.23 – 25 The most localized side effect of CSA is a transient burning sensation. However, several studies have not found any efficacy for CSA.26, 27 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.28

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.29 – 33

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.34

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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).44, 45

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.35

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

Surgery

Surgical excision, cryotherapy, CO2 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.44

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.41 – 43

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 trials. 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.44, 45

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.44, 45

Conclusion

No treatment has demonstrated convincingly its superiority over topical corticosteroid, the acceptable first-line choice mentioned in most reviews.46 – 50 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.44

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