ORIGINAL ARTICLE

Treatment modalities of oral lichen planus: an update

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Abstract:

Oral lichen planus is an immunologically based, chronic, inflammatory, mucocutaneous disorder of undetermined etiology. It is a relatively common disorder affecting stratified squamous epithelia. It is of special importance due to its malignant potential and can be a source of morbidity. The management of oral lichen planus should therefore address both the transformation rate as well as the patient symptoms. Care and management of such patients challenges even the most experienced clinician. There is currently no cure for OLP. Treatment is aimed primarily at reducing the length and severity of symptomatic outbreaks. The review critically analyses the various options in the literature and discusses the practical management from the Indian perspective.

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INTRODUCTION

Lichen planus is a dermatologic disorder which may involve various mucosal surfaces either independently, concurrently with cutaneous involvement, or serially. It frequently affects the oral mucosa more than the other mucosal sites. It is one of the more common mucosal conditions a clinician is likely to encounter in his clinical practice. The disease was first described by Wilson in 1869[1]. Globally, OLP affects about 1-2% of population and prevalence in India ranges from 0.1-1.5%. OLP can develop on any mucosal surface including larynx and oesophagus but lesions have predilection for the posterior buccal mucosa. The specific etiology of oral lichen planus is unknown. It is believed to result from an abnormal cell mediated immune response with infiltrating cell population composed of both T4 and T8 lymphocyte in the basal epithelial cells. They are recognized as foreign because of changes in the antigenicity of their cells surface[1].

It is unknown if lichen planus represents a single disease process or several closely related entities with similar clinical presentation. It can have many clinical presentations, ranging from, with some lesions requiring no treatment and others needing management for decades. Andreason in 1968 divided OLP into 6 clinical forms: reticular, papular, plaque like, atrophic, erosive and bullous[2]. The erosive and atrophic forms cause discomfort and painful symptoms. OLP is also of special importance due to its malignant potential[3]. The precancerous nature of oral lichen planus is still not settled, but patients must be carefully evaluated and observed. Presently, this condition is categorized as a "probable precancerous condition". After studying the status of oral lichen planus for several years, it was found that the occurrences of squamous cell carcinoma in most series ranged from 0.4 to 2.0% per five years observation period[4]. It is characterized by relapses and remissions, so its management should aim at resolution of painful symptoms, resolution of oral mucosal lesions, reduction of risk of oral cancer, and maintenance of good oral hygiene. In patients with recurrent painful disease, another treatment goal is the prolongation of their symptom free interval.

No treatment modality has been proved curative for OLP; switching on to the alternative agents used in the management of OLP suggests the inadequacy of any one agent to provide relief to the patient. This article reviews the different treatment modalities including drug therapy, surgery, psoralen with ultraviolet light A (PUVA), laser and natural alternatives used for the control of OLP.

Literature review of treatment modalities

Corticosteroids

Corticosteroids to date remain the first line of treatment for OLP because of their activity in dampening cell mediated immune activity there by modulating the immune function. These drugs can be administered topically, intralesionally or systemically. The most widely accepted treatment for lesions of OLP involves topical or systemic corticosteroids to modulate patient's immune response.

Topical corticosteroids are commonly used to treat mild to moderately symptomatic lesions, options include triamcinolone acetonide 0.1%, 0.05% flucinonide, 0.025% clobetasol propionate etc[5-7]. Patients are instructed to apply a thin layer of the prescribed topical corticosteroid upto 3 times a day. Topical aqueous triamcinolone acetonide suspension is proven to be effective in reducing mucosal erythema and ulceration[8]. In a study of 22 patients treated with 0.05% Flucinonide ointment in an orabase paste, approximately 60% improvement in symptoms after 2 weeks is noted[9]. Flucinonide in an adhesive base is considered as a safe and effective method to reduce signs and symptoms in OLP[10]. Lozada-Nur et al.[11] studied the efficacy of 0.025% clobetasol proprionate in treatment of OLP and other chronic oral vesiculo-erosive lesions and found it as an effective topical steroid alternative to other less potent topical and systemic drugs. Stomatopyrosis and hypoguesia was noted along with secondary candidiasis in this study. The advantage of topical steroid application is that side effects are fewer than with systemic administration. Adverse effects like secondary candidiasis, thinning of the oral mucosa and discomfort on application are seen with the use of these drugs. Prolonged use of potent topical corticosteroids with occlusal dressing can cause adrenal suppression.

Intra lesional steroid therapy

Persistent localized lesions are effectively managed by local injection of up to 0.2 to 0.4 ml of triamcinolone acetonide containing 10 mg/mL. Although initially painful, this technique maximizes drug delivery to the lesion while minimizing systemic absorption; side effects like muscular atrophy are seen to be associated with this therapy.

Systemic steroid therapy

Systemic steroids are usually reserved for moderate to severe OLP or in cases resistant to topical therapy. The most commonly prescribed systemic steroid to manage OLP is prednisone. The approach to therapy is to prescribe a high-dose, short-course regimen to maximize therapeutic effect while minimizing side effects. A single daily morning dose of 40 to 80 mg of prednisone is prescribed for no more than 10 days. The ultimate dosage chosen depends of the severity of the lesion and the size of the patient. The risk of the Hypothalamic-pituitary-adrenal axis (HPA-axis) suppression is negligible with such short-term bursts, thus tapering is not necessary. However, other possible

adverse side effects may occur and include insomnia, diarrhea, mood swings, nervousness, fluid retention, muscle weakness, hypertension, and decreased resistance to infection.

A prompt and impressive clinical response will be observed in the majority of patients undergoing systemic prednisone therapy. Once control is established, a topical agent should be introduced for maintenance and to reduce the risk of acute exacerbations. In the study by Silverman et al.[9] a much higher percentage of patients achieved a symptom free state with topical corticosteroid alone, then with either systemic corticosteroid or a combination of systemic and topical corticosteroids. Vincent et al.[8] did not show any significant improvement with the combination of systemic and topical corticosteroids, over topical corticosteroid used as a single agent.

Another approach to reduce the amount of total prednisone necessary is to concurrently prescribe a steroid-sparing agent such as the immunosuppressant drug azathioprine (50 to 100 mg/day) or levamisole (150 mg/day). Azathioprine appears to act synergistically with prednisone to reduce inflammation and allow for a lowering of the therapeutic prednisone dose. Possible side effects include nausea, vomiting, diarrhea, pancreatitis, bone marrow suppression, hepatotoxicity, arthralgias, and retinopathy. Levamisole in a dose of 150 mg/day and prednisolone 25 mg/day for 3 consecutive days each week for 4-6 weeks, showed improved results in the management of erosive OLP. Minor rashes, insomnia and head ache are few of the noted side effects[12,13].

In summary, many but not all patients can be managed with corticosteroids. Topical therapy should be maintained until symptoms and clinical findings improve. The decision to use cream, gel, or ointment is based on the practitioner's personal preference. Some may argue that gels tend to sting and burn, whereas ointments do not; however, gels adhere to the oral mucosa more easily than ointments. Regardless of shortcomings, they are both effective. Ulcerations that do not respond to topical agents can be injected with corticosteroids. Systemic corticosteroids should be reserved for acute exacerbations characterized by multiple ulcerations or widespread disease. Prolonged use of any of the above modalities without supervision will result in undesirable systemic effects and adverse local effects including candidiasis and atrophy.

Immunosuppressant - Cyclosporine

Cyclosporine is an immunosuppressant and reduces the production of lymphokines. This drug may be used topically or in the form of mouth rinse. Voute et al.[14] found no distinct advantages of cyclosporine over the use of topical corticosteroid. Cyclosporin can be used as an alternative therapy to conventional treatments for initial control of oral LP[15]. The cost of the drug and side effects such as hypertension and nephrotoxicity limits its use in the treatment of oral lichen planus.

Immunosuppressant - Tacrolimus

Tacrolimus is a macrolide immunosuppressant with a mechanism of action similar to cyclosporine, but is 10 to 100 times more potent and with better mucosal penetrating properties. Results from the study by Olivier et al.[16] suggest a rapid and important palliating effect of low concentration of topical tacrolimus in distilled water in patients with erosive OLP. Stoopler et al.[17] from their study concluded that topical use of tacrolimus is a safe, well tolerated, and effective therapy for oral lichen planus lesions recalcitrant to traditional therapies.

Retinoids

Retenoids have also been tried for the treatment of OLP. Previous studies revealed that side effects were common and troublesome with marginal improvement. In a study by Ferguson et al.[18] etritinate was found to have minimal value in the management of erosive OLP when used in dose of 25-75 mg for 8 weeks, with side effects such as pruritis, cheilitis, desquamation of hands and feet and paronychia. Meirgrosky et al.[19] in their study noted that when etritinate was used in the dose of 75 mg/day for 2 month it was effective in treating oral symptomatic lichen planus only for the duration of its use, discontinuation resulted in recurrence of signs and symptoms. Camisa and Allen[20] treated 6 patients with systemic isotretinoin (10 to 60 mg/day for 8 weeks) and concluded that it was of minimal benefit with common side effects, such as cheilitis, dry skin, headache, rashes etc. Topical application of Fenretinide (4-HPR), a newer retinoid showed to have a positive result with minimal side-effects in the treatment of OLP[21].

UV radiation

UV irradiation, especially in combination with psoaralens modulates the function of cells of the immune system. Lundquist et al.[22] used PUVA with methoxypsoaralen which produced a marked improvement in 9 out of 18 patients, with common side effects such as nausea, dizziness and sun sensitivity. Asko et al.[23] reported that topical trioxsalen photosensitization can be used in mouth PUVA treatment for the management of LP.

Griseofulvin

Griseofulvin has been advocated for the treatment of erosive-ulcerative lesions when steroid treatment is contraindicated or when the lesions are resistant to steroids. Aufdermorte et al.[24] administered 500 mg three times a day for 10 weeks and found it to be effective in all the 3 patients, whereas Bagan et al.[25]

did not find any improvement in 7 patients when similar dosage of griseofulvin was administered for 8 weeks.

Anti-malarials

Hydroxy-chloroquine sulphate showed positive results in management of OLP. 9 out of 10 patients showed excellent response to hydroxychloroquine when given in dosage of 200 to 400 mg daily as a monotherapy for 6 months. Use of anti-malarials have been discouraged in the management of OLP because of the possible lichenoid drug reactions[26].

Dapsone

Use of dapsone in the management of OLP has revealed some benefit, but disappointing results have been seen in gingival lesions. Generally the use of dapsone is precluded because of significant adverse effects like hemolysis, nausea and headache[27,28].

Phenytoin

It is an anti-epileptic drug with immunomodulatory and wound healing properties. 2 out of 4 oral lichen planus patients treated had complete healing by phenytoin therapy. No other studies to date have been carried out to confirm significance of these findings[29].

A recent systematic review by the Cochrane group[30] of all published reports of randomized placebo-controlled trials of palliative treatment for patients with symptomatic OLP concluded that there was only weak evidence that the evaluated treatment were superior to placebo. Specifically, 9 qualifying studies examining the effect of topical steroids, topical cyclosporine, and topical and systemic retinoids were analyzed. The authors of the review concluded that although most of the studies showed demonstrable treatment effects, the results should be interpreted with caution because of small sample sizes, lack of independent corroboration and difficulty in accurately measuring the results of treatment.

Photodynamic therapy

Photodynamic therapy (PDT) uses a photosensitizing compound like methylene blue which is activated at a specific wavelength of laser light. It is known to destroy the targeted cell via strong oxidizers, leading to membrane lysis, cellular damage, and protein inactivation. PDT has shown positive results in management of head and neck tumors. PDT have immunomodulatory properties which may induce apoptosis in the hyperproliferating inflammatory cells present in diseases like psoriasis and lichen planus, there by reversing the hyperproliferation and inflammation of lichen planus[31].

Surgical management

Surgical treatment is more applicable to the plaque-like lesions, because the affected surface epithelium can be removed easily. It may also be recommended in management of non healing erosions because it provides excellent tissue specimens for histopathologic confirmation of diagnosis. Surgical management is not suitable for the erosive and atrophic types because the surface epithelium is eroded. Cryosurgery and carbon dioxide laser therapies have been tried in management of OLP lesions. Inspite of several trials surgical treatment is not recommended due to the recurrence of inflammation[32,33]. Trauma from surgical procedures may induce new lesions via a Koebner phenomenon[34].

Natural alternatives

Lycopene

Use of lycopene, as a potent antioxidant in the management of various systemic and oral diseases including cancer and precancerous lesions has been reported in the literature. Supplementing with 8 mg/day of lycopene for 8 weeks showed favorable results in OLP patients. Burning sensation was reduced by 84% and lowered oxidative stress in a placebo-controlled trial[35].

Curcumin

Curcuminoids are components of *Curcuma longa* (turmeric) known to have anti-inflammatory properties. Studies to date indicate that higher dosages of curcumin (up to 6,000 mg/day) helped a significant number of OLP patients control their symptoms. Minimal side effects like diarrhea and gastrointestinal discomfort may occur, which are usually dose related. Whereas smaller doses of curcumin (< 2,000 mg/day) have failed to provide relief[36,37].

Green Tea

Green tea (epigallocatechin-3-gallate) is known to have possessing anti-inflammatory and chemopreventive properties. It is known to reduce the incidence of OLP by regulating the factors which are involved in the etiopathogenesis of the disease. Green tea is known to inhibit T-cell activation, migration, proliferation, antigen presentation and control other inflammatory mediators[38].

Aloe vera

Various studies reveal that orally applied aloe vera reduces pain, promotes remission and improves quality of life in patients living with OLP. In a study by Salazar-Sánchez et al.[39], 64 patients with OLP were randomized in a double-blind study; 32 patients were treated with aloe vera dose of 0.4 ml (70% concentration) three times a day and placebo 32 patients

were given placebo. 61% patients treated with aloe vera showed complete pain remission after 12 weeks. In the placebo group, this percentage was 41.6%. There were no adverse effects in any of the groups. There by improving total quality of life score in patients with OLP. A randomized, double-blind, placebo. In-controlled trial of 54 patients into two groups was done by Choonhakarn et al.[40] where patients were given aloe vera gel or placebo for 8 weeks. 22 patients treated with aloe vera had a good response after 8 weeks of treatment, 2 patients treated with aloe vera had a complete clinical remission. Burning pain completely disappeared in 9 patients treated with aloe vera.

Ignatia

Ignatia, a homeopathic medicine, is an all-natural and gentle alternative. In a single blind randomized control clinical trial[41], 30 consecutive OLP patients were administered Ignatia 30C (a measure of homeopathic potency) or placebo for 4 months. Patients treated with Ignatia showed decrease in pain and in the size of the mean lesions in comparison to placebo group.

CONCLUSION

Patients with OLP should be counseled as per the nature of this chronic condition and the different approaches to treatment. Even though evidence of the efficacy of these treatment approaches is not overwhelming, corticosteroid therapy remains the most common approach for managing symptomatic lesions. Because of the possibility of increased risk of malignant transformation, periodic reassessment of all patients with OLP is recommended.

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