Recent Update on Treatment Modalities of Oral Lichen Planus – A Review

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Lichen planus is a chronic, noninfectious, inflammatory, and autoimmune disease of the skin and mucous membrane. Intraorally, the buccal mucosa, tongue, and gingiva are the sites commonly involved. It affects women more often than men in a ratio 3:2. It has well-recognized clinical signs and symptoms, the symptoms may range from none, through mild discomfort to a severe burning sensation. The oral lesions are more resistant to therapy and there is less spontaneous remission compared to cutaneous form. Patient education may improve the outcomes of oral lichen planus (OLP) therapy and further reduces the risk of oral cancer. For the accurate diagnosis of the OLP following criteria’s are required: (i) Assessment of causative or exacerbating factors, associated diseases and oral cancer risk; (ii) patient education and management; (iii) histological diagnosis; (iv) medical treatment; and (v) long-term review and re-biopsy as required. Choice of treatment may vary depending on the severity of the lesion and systemic condition of the patient. Treatment is administered mainly to resolve symptoms and discomfort. A variety of agents have been employed for the management of OLP, but corticosteroid remains the mainstay of treatment. Given the fact that for atrophic and erosive forms of OLP bears malignant transformation rate, so the patients need to be actively treated and kept on long-term follow-up. The main objective of this paper is to review the current literature regarding the treatment of OLP.

Keywords: Immunomodulators, Management, Malignant transformation oral lichen planus, Steroids

INTRODUCTION

Oral lichen planus (OLP) is a chronic autoimmune, mucocutaneous disease of unknown origin. It was first described by Wilson in 1869. It can affect the oral mucosa, skin, genital mucosa, scalp, and nails. Globally, Lichen planus affects about 1-2% of population and prevalence in India ranges from 0.1% to 1.5%. This disease has most often reported in middle-aged patients 30-60 years of age and is more common in females than in males (1.4:1). Rarely, OLP is seen in children.

It is believed that the disease is caused by an abnormal cell-mediated immune response of both T4 and T8 lymphocytes in the basal epithelial cells. Autocytotoxic CD8 + T-cells activate apoptosis of oral epithelial cells. The CD8 + cytotoxic cells trigger the keratinocyte apoptosis through activation of the cells by an antigen associated with major histocompatibility Class I on basal keratinocytes. The chronic course of OLP may result from the activation of the inflammatory mediator nuclear factor kappa B, and the transforming growth factor control pathway may cause keratinocyte hyper proliferation that leads to the white lesion.

OLP may be associated with many systemic diseases, few have been confirmed, but infection with hepatitis C virus (HCV) can produce lichen planus. Carrozzo et al. have demonstrated a strong association between HCV infection and OLP. However, the association between OLP and HCV appears to be dependent on geographical heterogeneity. Moravvej et al. in 2007 found an association between Helicobacter pylori infection and lichen planus patients. However, an etiologic role of H. pylori in lichen planus is not yet properly established.

Anderson in 1968 divided OLP into 6 clinical forms: Reticular, papular, plaque-like, atrophic, erosive, and bullous. Oral lesions present as white striations (whickham striae), white papule, white plaques, white papules, erythema (mucosal atrophy), erosions (shallow ulcers), or blisters. The lesions mainly affect the buccal mucosa which is usually bilateral,
tongue, and gingiva. About 10% of patients with OLP have disease confined to the gingiva. Lesions on the palate, the floor of mouth and lip are uncommon. Cutaneous lesions may be encountered in approximately 15% of patients with OLP. The classic appearance of skin lesion consists of pruritic erythematous to violaceous papules that are flattopped that have predilection for trunk and flexor surfaces of arms and legs.

Approximately, two-thirds of OLP patients report discomfort, especially in association with erosive and atrophic LP. A greater malignant potential has been found for these two forms of LP and plaques formed on the posterior aspect of the tongue. After studying the status of OLP for several years, it was found that the occurrence of squamous cell carcinoma ranged from 0.4% to 2.0% per 5 years observation period. Mignona et al. have suggested regular follow-up of patients with OLP should be performed up to 3 times a year. OLP with dysplasia should be examined more frequent, and follow-up should be done in every 2-3 months.

Lichen planus characterized by relapse and remissions, so its management should aim at the resolution of painful symptoms, oral mucosal lesions, the risk of oral cancer and the maintenance of good oral hygiene. In patients with the recurrent painful disease, another treatment goal is the prolongation of their symptom-free interval by continuing the treatment therapy.

The aim of this article is to review and evaluate the various treatment modalities and measures that have been reported in the management of patients with OLP.

CORTICOSTEROIDS

To date, corticosteroids remain the first choice of treatment for OLP, it has been found to be the most expected and successful agents in the treatment of OLP.

The efficacy of corticosteroids for treatment of lichen planus is mainly attributed to its anti-inflammatory and immunosuppressive actions. They induce varied metabolic effects, modify the body’s immune response to diverse stimuli and decreases inflammation by reversing the increased capillary permeability and by suppressing polymorphonuclear neutrophils activity. They can be used topically, intralesionally, or systemically.

TOPICAL STEROID THERAPY

High-potency topical corticosteroids in an adhesive medium appear to be the safest and most effective treatment of mild to moderately symptomatic lesions. For topical applications, they are prescribed as gels, creams, ointment with Orabase (Kenalog in Orabase®), or oral rinse.

Various topical steroids are available, these are clobetasol propionate gel, 0.05%; betamethasone valerate gel, 0.1% or 0.05%; fluocinonide gel, 0.05%; clobetasol butyrate ointment or cream, 0.05%; and triamcinolone acetonide ointment, 0.1%. The patients are instructed to apply a thin layer of the prescribed topical corticosteroid up to 3-4 times a day. The patients are advised not to eat or drink for 30 min after the application. Topical aqueous triamcinolone acetonide suspension is proven to be effective in reducing mucosal erythema and ulcerations. The advantage of topical steroid application over systemic administration is that side effects are fewer.

Prolonged use of topical steroids over ulcerated areas may lead to local complications such as blanching of the mucosa, hypopigmentation of the applied area, delayed wound healing with increased friability of the mucosa, and often systemic complications such as, Cushing’s syndrome, reversible hypothalamic-pituitary-adrenal (HPA)-axis suppression, hyperglycemia, or glycosuria. This is due to rapid absorption of steroids from denuded areas of oral mucosa which leads to its highest tolerable levels within a short span of time.

Ahadian et al. in 2012 conducted a study on comparison of two corticosteroids mouthwashes, i.e., dexamethasone (0.1%) and triamcinolone (0.2%) in the treatment of 44 symptomatic OLP patients for 4 weeks and concluded that both mouthwashes were useful in reducing pain and decreasing the size of the lesion. However, in comparison of both the mouthwashes, dexamethasone mouthwash was said to be more effective.

Intra-lesional Steroid Therapy

Intra-lesional injection of corticosteroid for severe lesions involves the subcutaneous injection of 0.2-0.4 mL of a 10 mg/mL solution of triamcinolone acetonide (Avocort® injection, Comcort® injection) by means of a 1.0 ml 23- or 25-gauge tuberculin syringe. Although initially painful, this technique maximizes drug delivery to the lesion while minimizing systemic absorption. Main drawback of intra-lesional corticosteroids use is atrophy of tissues, secondary candidiasis, and difficulties into gingival lesions.

Systemic Steroid Therapy

Indicated at high dose (1.5-2 mg/kg/day) for patients with recalcitrant severe erosive atrophic OLP where topical approaches have failed or for diffuse mucocutaneous involvement. However, adverse effects are possible even with short courses. The most common prescribed systemic steroid to manage OLP is prednisone. A single daily
morning dose of 40-80 mg of prednisone is prescribed for 10 days. The ultimate dosage chosen depends on the severity and size of the lesion.\(^4\)

If corticosteroids are used for prolonged therapy, they should not be stopped abruptly because it can flare up the underlying disease for which steroids were prescribed and cause acute adrenal insufficiency due to HPA axis suppression.\(^3\) However, other possible adverse side effects may occur such as insomnia, diarrhea, mood swings, nervousness, fluid retention, muscle weakness, hypertension, and decreased resistance to infection.\(^4\)

A prompt and impressive clinical response will be observed in the majority of patients undergoing systemic prednisone therapy. Once, the symptoms resolved a topical agent should be introduced for maintenance and to reduce the risk of acute exacerbations. In Silverman et al. study, a much higher percentage of patients achieved a symptom-free state with topical corticosteroid alone than with either systemic corticosteroid or a combination of systemic and topical corticosteroids.\(^3\)

Another approach to reduce the amount of total prednisone is to prescribe a steroid-sparing agent such as the immunosuppressant drug azathioprine (50-100 mg/day) or levamisole (150 mg/day). The azathioprine appears to act synergistically with prednisone to reduce inflammation and combination dose also allow for a lowering the therapeutic dose of steroids. The 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.\(^5\)

**IMMUNOSUPPRESSANT**

These agents modulate the immune system. It induces a substantial decrease of T-cells and a corresponding reduction in activated CD25-positive cells and in antigen presenting cells possibly by inhibition of interferon-gamma production.\(^5\)

**Cyclosporine**

It is a very commonly used immunosuppressant drug that belongs to a family of cyclic polypeptides derived from the fungus *Tolypocladium ianflatum*. It is basically used to prevent rejection of organ transplantation. The topical cyclosporine can be used either in the form of mouthwashes or in the form of adhesive base. The patients are advised to swish and spit 5 ml of mouthwash, i.e. 100 mg cyclosporine/ml 3 times daily for 4 weeks or 0.025% cyclosporine in an adhesive base to apply 4 times daily.\(^13,14\)

Systemic treatment has been used in severe resistant cases and in oral-cutaneous or ulcerative foot involvement. For adults, 1-2 mg/kg/day PO is the recommended starting dosage and if no response in disease pattern, the dosage can be increased to 5 mg/kg/day. The cyclosporine is available in 25, 50 mg capsule (Immusol\(^9\), Immuspiron\(^8\)), 100 mg/ml oily solution (Katzung\(^9\)), and 100 mg/ml oral rinse (sandimmun neoral\(^9\)).

Renal and liver functions have to be assessed before usage since the drug is hepatotoxic and nephrotoxic. Other adverse effects include hypertension, gingival enlargement, hyperkalemia, hypomagnesemia, pancreatitis, and paresthesia. Due to the severe adverse effects and the oral lesions being often chronic in nature, the usage is limited.\(^5\)

**Tacrolimus**

It is a macrolide form of immunosuppressant derived from a type of bacterium, *Streptomyces tsukubaensis*. Initially, it is used to prevent organ rejection in kidney transplantation.\(^13\)

It inhibits the T-cell production of pro-inflammatory cytokines. The topical application induces a rapid improvement in OLP.\(^5\) it is 100 times more potent than cyclosporine, has shown to be effective without notable side effects in several uncontrollable studies.\(^8,17\) It has greater percutaneous absorption than cyclosporine. Its systemic use is comparable to the corticosteroids, but topical application of 0.1% tacrolimus is proved to be superior in treating symptoms of OLP. Recent studies by Corrocher et al. have shown that application of tacrolimus ointment 0.1% 4 times daily for 4-8 weeks resulted in faster resolution of symptoms as compared to the corticosteroids.\(^13\) Malik et al. in 2014, successfully treated a case of OLP with 1% of tacrolimus powder with base 3 times daily for 15 days in a patient with raised SGOT, SGPT levels along with positive tri-dot for HCV.\(^18\)

**Pimecrolimus**

It inhibits the T-cell activation by inhibiting the synthesis and release of cytokines from T-cells. It also prevents the release of inflammatory cytokines and mediators from mast cells. 1% topical cream of pimecrolimus has been successfully used as the treatment for OLP. It has a significant anti-inflammatory activity and immunomodulatory capabilities with low systemic immunosuppressive potential.\(^19\)

**Levamisole**

It is an effective immunomodulating agent that can restore the normal phagocytosis activity of macrophages and neutrophils.\(^5\) It was developed in 1966 as an anti-helmithic drugs but has immunoregulating properties.\(^13,14\)

The levamisole is an effective drug in steroid resistant and the patients who have not responded to conventional treatments.\(^5\) The levamisole is administered at a dose of 50 mg 3 times/day for 3 consecutive days per week for
4-6 weeks. It is available as 50 mg and 150 mg tablet. (Ergamisole® and Vermisole®). It has an adverse effect such as nausea, vomiting, headache, and agranulocytosis. 13

Azathioprine
It is a purine antimetabolite having anti-inflammatory properties and decrease antibody production. It is reserved for the patients who are not responding for the other treatment modalities. It can also be used in combination with corticosteroids and cyclosporines. In combination, it effectively decreases the immunosuppressive activity. So, lower doses of corticosteroids can be used. It is available in the 50 mg tablet (Imuran®, Azoprin®). 5,8,13,14

Retinoids
The use of retinoids was 1st reported by Gunther et al. in 1973. 1 The retinoids are a class of chemical compounds that are related to vitamin A, and its main function is to regulate epithelial cell growth. 5

The topical and systemic forms of retinoids have been used in the treatment of OLP. 1 Both systemic and topical retinoids should be used as an adjuvant therapy only. First generation compound includes retinol and compounds derived from it metabolically – Tretinoin and isotretinoin. Second generation retinoids are synthetic analogs, i.e., etretin and acitretin. Third generation retinoids include arotinoids, which are currently in development. 13 The topical retinoids such as tretinoin, isotretinoin, and fenretinide, with their immunomodulating properties have been reported to be effective in OLP. 13,18

It is studied that topical 0.1% vitamin A rapidly eliminated white lesions of OLP but all the cases relapsed after 2-5 weeks of cessation of therapy. 13 Very recently, a new topical retinoids, tazarotene has been used for the treatment of OLP and demonstrated to be helpful in hyperkeratotic OLP. 2

Dapsone
In resistant cases of erosive, OLP dapsone is an effective with anti-inflammatory and immune-modulatory effects. It is available as 5% gel (acnesone®) for topical application and systemically 25, 50, and 100 mg of tablets. Headache and hemolysis are significant side effects of dapsone. 13

Interferon
The topical application of human fibroblast interferon gel and interferon-alpha have suggested to improve erosive OLP. 13

PUVA Therapy
Photosensitizing psoralen drugs and ultraviolet A (UV) radiation were introduced as a new therapy by Jansen et al. in 1987 for oral mucosal lesions. The photosensitizing drugs can either be administered systemically or applied topically before irradiation. Four psoralens are used in PUVA therapy – psoralen, 5 methoxy psoralen (Bergapten®), 8-methoxypsoralen (methoxsalen®), and 4,5,8 trimethyle psoralen (trioxsalen®). UV irradiation in combination with psoralens modulate the function of cells of the immune system. 13,14

NATURAL ALTERNATIVES

Lycopene
The lycopene is a potent antioxidant in the management of various systemic and oral diseases including cancer and precancerous lesions and conditions. 8 mg/day of lycopene for 8 days showed significant improvement in the OLP lesions. Burning sensation was reduced up to 84% of cases. 4

Curcumin
It is a component of curcuma longa, i.e., turmeric having anti-inflammatory properties. Higher doses of curcumin up to 6000 mg/day helped to reduce the symptoms of OLP with the minimal side effects such as diarrhea and gastrointestinal tract discomfort. 4

Green Tea
It possesses both anti-inflammatory and chemopreventive properties. It inhibits the T-cell activation, migration, and proliferation and also controls other inflammatory mediators. It is known to reduce the symptoms of OLP by involving in the etiopathogenesis of the diseases. 4

Aloe Vera
Oral application of aloe vera reduces the pain, promotes the remission and improves the quality of life of OLP patients. 4

Photodynamic Therapy
Photodynamic therapy is a technique that uses a photosensitizing compound with the specific wavelength of laser light to destroy the targeted cell via strong oxidizers, which causes cellular damage, membrane lysis, and protein inactivation. The photodynamic therapy with Parenteral Drug Association the approved drug methyle 5-aminolevulinate OLP offers a single treatment with long lasting improvement. PDA has an immunomodulatory properties, it induces apoptosis in the hyper proliferating inflammatory cells present in the disease such as psoriasis and lichen planus. 4,12,20-22

Surgery and Lasers
Surgical excision, cryotherapy, CO2 laser, and neodium-doped yttrium aluminium garnet laser have all been used in the treatment of OLP. It is more applicable in plaque type of OLP because the affected surface epithelium can be removed.

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CONCLUSION

The management of OLP should begin by taking the proper history and clinical examination. Elimination of any form of irritants-like maloccluded teeth, ill-fitting dentures, amalgam fillings should be removed. Incisional biopsy should be done to confirm the diagnosis. The patients with erosive or atrophic forms particularly should be observed periodically as it has malignant transformation potential varying between 0.3% and 3%. For the effective management of OLP, one has a wide range of drugs to choose from. When a patient with OLP presents with a burning sensation, usually as a first line of treatment one can prescribe a topical preparation of steroid and retinoids. As a second line of treatment in cases of steroids resistant, we may prescribe immunomodulatory drugs such as levamisole and dapsone. In resistant cases, where it is not responding to topical preparations or in a severe form of OLP tacrolimus, and systemic corticosteroids in conjunction with immunosuppressive like azathioprine can be given. So, it is essential to choose appropriate drug, mode of administration and dosage regimens individually and equal importance should be given for stress management. One should not forget the relationship between stress and inflammatory skin diseases. Regular relaxation exercises, meditation and hypnosis help to calm and rebalance inflammatory response which can ameliorate inflammatory skin disorders. Continuous development in management protocol for OLP is required due to recent increase in the incidence of malignant transformation rate even in the non-risk population group.

REFERENCES


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