International Journal of Contemporary Dental Research (IJCDR)
Vol. 01, Issue. 2, Apr 2023, pp. 27~30
ISSN –2584-0274 DOI: https//doi.org/10.62175/apdch2312

Management of Oral Lichen Planus: Recent updates

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Article Info

Article history:

Received:01/08/2023
Revised: 02/17/2023
Accepted: 03/25/2023

Keywords:

Oral lichen planus,
treatment,
steroids

ABSTRACT

Oral lichen planus is one of the most common dermatological disease affecting the oral mucosa. It is characterized by periods of remission and exacerbation. Regular follow up is needed for some severe forms of oral lichen planus. Various treatment modalities are reported in the literature and this article discusses about some of the recent medications used in patients with oral lichen planus.

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1. Introduction:

Oral lichen planus (OLP) is a T cell mediated chronic inflammatory disease that affects oral mucosa.[1] Apart from oral mucosa, lichen planus also affects the skin, nails, hair, genitals, gastrointestinal and ocular mucosa.[2] .The exact etiology of OLP is unknown and hence, there is no specific treatment plan for this disease. However, there are some therapeutic approaches found to be effective. Oral lichen planus probably represents a cell mediated immunologic response to an induced antigenic change in the oral mucosa[3,4]. The possible association of OLP with anxiety, depression and stress has also been reported.[5]

Pathogenesis:

Pathogenesis of oral lichen planus includes antigen specific and non-specific inflammatory mechanisms. Cytotoxic CD8+ Tcells trigger apoptosis of the basal layer of the epithelium.[6] Cell mediated immune response starts with keratinocytes antigen expression. This is followed by migration of T lymphocytes which has been activated by an antigen binding to the major histocompatibility complex (MHC 1) on keratinocytes or through activated CD4+ lymphocytes.[7]Activated T cells also kills basal keratinocytes through tumor necrosis factor (TNF α),Fas-FasL-mediated or granzyme B-activated apoptosis.Non-specific mechanisms further aggravate the T-cell accumulation. The basement membrane disruption occurs by mast cell proteases and keratinocyte apoptosis.[8]

Clinical features:

This disease most commonly affects middle aged women, ranging between 30-60 years of age.[4] The clinical subtypes of oral lichen planus are reticular, plaque-like, atrophic, erosive/ulcerative, papular, and bullous form. Among these, reticular, erosive /ulcerative and plaque like subtypes are most common in the oral cavity [9].Most common sites affected are buccal mucosa, gingiva, tongue, and mucobuccal folds.[10]. Reticular lesions are usually asymptomatic and they appear as a network of interlacing white striae. Erosive or ulcerative types produce discomfort to the patients and they appear as erythema and ulcerations of varying sizes.[11,12] Plaque like lesions appears as white, homogenous slightly elevated, smooth areas. A definite diagnosis of lichen planus cannot be made by clinical examination. WHO proposed a set of clinicopathologic

criteria for diagnosing oral lichen planus.[9]Hence, the diagnosis of oral lichen planus should be made based on both clinical and histopathologic examination.

Management:

Treatment of oral lichen planus should be done based on the clinical condition, psychological state and medical history of the patient[11]. In the literature, systemic therapy has been proposed to control exacerbation of oral lichen planus, but topical application of medication is found to be easiest to practice. Hence, it is considered as the first line of treatment.[13]

1. Corticosteroids:

Corticosteroids are the most important agents in treating oral lichen planus. They can be prescribed topically as well as systemically. According to Vaishnavi devi *et al*, triamcinolone is the most commonly prescribed corticosteroid.[14]The topical agents generally used are 0.1% triamcinolone acetonide, 0.025% clobetasol propionateand 0.05% fluocinonide.[3]

Prednisolone is the 2nd preferred corticosteroid. Prednisolone is mainly used as systemic steroid .They act by reducing the infiltration of lymphocyte and stabilizes lysosomal membrane. Some researchers suggest that combination therapy of both systemic and topical corticosteroid is effective in many patients. Even though topical application is easier, long term use of topical steroid leads to oral candidiasis. In oral cavity the salivary flow will constantly wash off the topical steroids.The short retention time of the drug leads to low therapeutic efficacy. In order to resolve this limitation some bioadhesive formulations of dosage forms are also available. Main disadvantages of this type of local drug delivery are minimal surface area of mucosa, minimal exposure time, and unpleasant taste.[14]

Intralesional injectionsare effective in the treatment of OLP, especially if patient does not respond to topical applications. Lodi *et al*. reported an higher efficacy of steroid injections, and confirmed that triamcinolone is the most effective drug.[15,10].Thongprasom*et al* reported that intralesional injection of steroids gave variable results and they are painful and have localized side effects such as mucosal atrophy.[16]

2. Calcineurin Inhibitors:

Calcineurin inhibitors include cyclosporin, pimecrolimus and tacrolimus. Patients with desquamative gingivitis or diffuse ulcerations, may not respond to topical corticosteroids alone. In such patients immunosuppressants or immunomodulatory agents such as cyclosporine, tacrolimus, pimecrolimus, in topical formulations may be useful.[12, 13] Cyclosporins can be used as mouth rinses but is very expensive for routine use.

Tacrolimus is a steroid free topical immunosuppressive. Hodgon *et al* reported that 14% of the oral lichen planus patients in their study show complete resolution of ulcers and erosions when tacrolimius was applied over a period of 19 months.[12]

Application of Pimecrolimus 1% cream also has been reported to show improvement in lichen planus lesions[13]. The most common side effects associated with this therapy are hyperpigmentation of the mucous membranes, burning sensation immediately after application, xerostomia and gastrooesophageal reflux.[17]

3. Retinoids:

Topical and systemic retinoids such as tretinoin, isotretinoin and fenretinide are found to be effective in treating oral lichen planus. Systemic isotretinoin is particularly used in treating erosive lichen planus. Due to the possible side effects of systemic retinoids and also due to low remission rates, primary use of retinoids is discouraged. They can be used as an adjuant therapy only.[10]

4. Amlexanox:

Amlexanox is a topical anti-inflammatory drug. It inhibits the formation and release of histamine, TNF-α and leukotrienes from mast cells, neutrophils and mononuclear cells.[5]

5. Lycopene:

Lycopene is a fat-soluble carotenoid which has antioxidant activity. It inhibits cancer cell proliferation and growth factor stimulation. Lycopene is found to reduce burning sensation in oral lichen planus patients.[18]

***6.* Herbal modalities:**

a. *Curcumin:* Curcuminoids are components of turmeric, which exhibits anti-oxidant, anti-inflammatory, anti-microbial and anti- carcinogenic activity. Curcumins will reduce the incidence of oral lichen planus by regulating the factors involved in their etiopathogenesis.[19]

b. *Alovera gel*: Aloveragel has various biological properties like anti-oxidant and anti-inflammatory action by virtue of its cyclooxygenase inhibition properties and decreases leukocyte adhesion molecule and tumor necrosis factor alpha levels. Studies has shown that alovera gel produce a good result in oral lichen planus patients.[19]

c.*Tulsi:* Tulsi has an ability to prevent the effects of metabolic stress by normalization of blood glucose, lipid levels, blood pressure and psychological stress through positive effect on memory and cognitive function. This properties of tulsi with its pharmacological actions promote wellbeing and resilience and hence, tulsi can be used in treating OLP.[19]

d.*Black pepper*: Black pepper contain piperine that can be used as a supplementory therapy in oral lichen planus patients. Piperine has inhibitory effects on antigen-specific mechanisms and the overproduction of COX-2 as well as enhanced oxidative stress. It also prevent carcinogenesis in oral lichen planus.[20]

7. Non Pharmacological treatments:

a. ***Photodynamic therapy***: It is a non-invasive therapy for OLP. Photo dynamic Therapy uses a photosensitizing compound like methylene blue which is activated at specific wavelength of laser light.This interaction produces free radicals and leads to cell damage. In the literaturevarious studies were reported in the qualitative and quantitative analysis. In these studies the authors concluded that photodynamic therapy is very effective as topical corticosteroids and can be used for oral lichen planus patients who were resistant to corticosteroids or in cases when they are contraindicated. A decrease of CD4+, CD8+ and IL-17+ cells in the oral mucosa affected by OLP has been reported after photodynamic therapy.[2]The side effects of photodynamic therapy are local skin reaction like erythema, edema and desquamation.[11]

b. *PUVA therapy*: It is a photochemotherapy with 8-methoxypsoralen and long wave ultraviolet light. Methoxypsoralen is given orally, followed by administration of 2 hours of UV radiation intraorally in the affected site. This protocol has shown encouraging results in the treatment of severe cases of oral lichen planus.PUVA causes photoconjugation of psoralen to DNA and causes suppression of mitosis, DNA synthesis, and cell proliferation. These effects are specific to lymphocytes or PMNL.The adverse effects include nausea and dizziness secondary to psoralen.[4]

c.*Low level laser therapy*: Low-level laser includes various light sources such as helium neon (633nm), ruby (694nm) and argon (488and514nm).Photobiomodulation has a beneficial effect on cell metabolism without damaging cells of the body.Deep penetrating lasers damages the inflammatory cells of connective tissue. It alsomodulate mast cells, decrease prostaglandins and increase the production of basic growth factors.Laser treatment tends to be more effective in treating painful erosive OLP.[8]

2. Conclusion:

In patients with oral lichen planus, a generalised treatment protocol cannot be given. The treatment modalities may vary from patient to patient. Topical corticosteroids remain the first line treatment for this disease. For some severe cases, systemic therapy or combined therapy is necessary. When initial therapies become non-responsive, other non-pharmacological therapies can be used.

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