

NEW TREATMENT APPROACH IN ORAL LICHEN PLANUS

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Abstract : Oral lichen planus is a chronic autoimmune mucocutaneous disease that is relatively common disorder mediated by T lymphocytes affecting oral and genital mucous membranes, skin, nails, and scalp. Although many patients are asymptomatic and require no therapy, those who exhibit atrophic and erosive lesions are often a challenge to treat. Since the etiopathology of OLP is idiopathic, treatment is usually symptomatic, therefore showing low predictability. Currently employed treatment modalities include corticosteroids administered topically, intralesionally, or systemically. Alternative therapies include topical and systemic retinoids, Cyclosporine. Other medical treatments and experimental modalities, including mouth PUVA, have been reported to be effective. In this review, we discuss the current treatment modalities of OLP since last 20years.

Keywords : Oral Lichen Planus, Autoimmune, T-lymphocytes

INTRODUCTION

Lichen planus (LP) is a chronic, autoimmune mucocutaneous disorder mediated by T lymphocytes affecting oral and genital mucous membranes, skin, nails, and scalp [1]. It is estimated to affect 0.5%–2.0% of the general population[5]. Females are twice as likely to be affected and the incidence peaks at age 50 [2–4]. Oral lichen planus (OLP) is the mucosal counterpart of cutaneous LP. It occurs more frequently than the cutaneous form and tends to be more persistent and more resistant to treatment [1–4].

Andreasen (1968) divided oral lichen planus into six clinical forms, including reticular, papular, plaquelike, atrophic, erosive, and bullous. A simpler classification system we have devised involves grouping reticular, papular, and plaquelike oral lichen planus into reticulated lesions, which usually are asymptomatic. Erosive (including bullous) lesions and atrophic (erythematous) lesions are distinct forms that are usually a source of pain and discomfort. Desquamative gingivitis, a clinically descriptive term that encompasses many diseases, can apply to conditions characterized by clinically atrophic lesions with histologic oral lichen planus.[6]

RECENT CONCEPT IN TREATMENT

1] Corticosteroids

The most widely accepted treatment for lesions of OLP involves topical or systemic corticosteroids to modulate the patient's immune response.

Topical corticosteroids -

Topical corticosteroids include 0.05% clobetasol propionate gel, 26 0.1% or 0.05% betamethasone valerate gel, 6 0.05% fluocinonide gel, 27 0.05% clobetasol butyrate ointment or cream, and 0.1% triamcinolone acetonide ointment. In which patients are instructed to apply a thin layer of the prescribed topical corticosteroid up to 3 times a day, after meals and at bedtime. The gel or ointment can be applied directly or can be mixed with equal parts Orabase (a gelatin–pectin–sodium carboxymethylcellulose-based oral adhesive paste, ConvaTec, Division of Bristol-Myers Squibb, Montreal, Que.) to facilitate adhesion to the gingival tissues.[7]

In patients with widespread symptomatic lesions, in whom direct mucosal application of topical medication would be too uncomfortable, options include 1.0 mg/mL aqueous triamcinolone acetonide or 0.1 mg/mL dexamethasone elixir. Patients should be instructed to gargle with 5 mL of the solution for 2 minutes after meals and at night. After rinsing, the solution should be expectorated, and nothing should be taken by mouth for one hour.[7]

Alternative delivery methods include the use of cloth strips and custom trays to serve as reservoirs for the corticosteroid.[7]

Another study done to evaluate efficacy and compliance of new lipid microspheres loaded with 0.025% of clobetasol propionate (formulation A) compared with a commonly used formulation (a sort of dispersion of a lipophilic ointment in a hydrophilic phase) with the same amount of drug (formulation B) in the topical treatment of OLP. results suggest that the new topical drug delivery system (formulation A) may enhance, at least in terms of symptom remission and compliance, the effectiveness of clobetasol propionate at a dose of 0.025% in OLP therapy.[9]

Systemic steroid

Intralesional injection of corticosteroid 0.2–0.4 mL of a 10 mg/mL solution of triamcinolone acetonide by means of a 1.0-mL 23- or 25-gauge tuberculin syringe subcutaneously given for recalcitrant or extensive lesions by means of a 1.0-mL 23- or 25-gauge tuberculin syringe.[8]

2] Topical Tacrolimus

Topical tacrolimus application to mucosal lesions is an innovative treatment approach. Tacrolimus ointment was used at a concentration of 0.1%; patients were instructed to self-administer tacrolimus ointment twice daily to the affected mucosal lesions with a cotton swap or sterile gauze. Objective assessment of response to topical tacrolimus by a clinician revealed an objective response of 100% and a 55% complete remission rate with disappearance of all erosive/ulcerative mucosal lesions after the eight-week study period. So Topical tacrolimus ointment is a safe and very effective treatment approach for erosive lichen planus and deserves further investigation.[10]

Twice-daily topical application of compounded 0.1% tacrolimus ointment was recently reported to be effective in controlling symptoms as well as clearing lesions of OLP.[11,12] Tacrolimus is a macrolide immunosuppressant with a mechanism of action similar to that of cyclosporine, but is 10 to 100 times more potent and is better able to penetrate the mucosal surface.[12]

3] Hydroxychloroquin

Hydroxychloroquine is an antimalarial drug having anti-inflammatory and immunomodulatory properties, which are helpful in treating LP by reducing the cytokine production, so that inflammation is reduced. Hydroxychloroquine has inhibitory action on Toll-like receptor 9, which is required for maturation of dendritic cells, thereby reducing the inflammation. A proper treatment plan, based on the type and severity of the disease, can prove to be beneficial, thereby improving patient care for those suffering with OLP as well as improving the quality of life. HCQ can be a promising drug in treating OLP and holds great potential for more research and trials related to this treatment modality.[17]

4] Cyclosporine

Cyclosporine, a calcineurin inhibitor, is an immunosuppressant used widely in post-allogenic organ transplant to reduce the activity of patient's immune system. This selectively suppresses T-cell activity, the main reason for transplant rejection, and hence enhances the uptake of the foreign organ. Cyclosporine binds to the cytosolic protein cyclophilin of immunocompetent lymphocytes, especially T-lymphocytes. This complex of cyclosporine and cyclophilin inhibits calcineurin, which under normal circumstances induces the transcription of IL-2. They also inhibit lymphokine production and IL release, leading to a reduced function of effector T-cells. Cyclosporine is used as a mouth rinse or topically with adhesive bases in OLP. However, the solution is prohibitively expensive and should be reserved for highly recalcitrant cases of OLP. Systemic absorption is very low. It is known to cause dose-related gum hyperplasia which reduces when the drug is withdrawn.[20]

5] Zinc Therapy

Nallan CSK Chaitanya et.al.revealed that oral zinc acetate 50 mg twice daily may be an effective treatment modality in patients of oral lichen planus. Significant decrease in burning sensation, pain, and lesion size was observed which may be explained by the anti-inflammatory and Wound-healing-properties.[24]

Mehdipour *et al.* compared the efficacy of combination of 0.2% zinc mouthwash with fluocinolone with fluocinolone monotherapy in the treatment of oral lichen planus and found that combination of 0.2% zinc mouthwash with fluocinolone was more effective in decreasing the lesion surface area, pain, and burning sensation probably owing to the role of zinc in healing the disrupted epithelium.[25] Zinc helps in regeneration and repair of epithelium, strengthens the local defense system thus leading to reduction in inflammation and bacterial growth. Zinc also has a role as a cofactor in numerous transcription factors which may explain its regenerative properties.[26]

6] Topical retinoids

Topical retinoids appear as an alternative choice in OLP treatment. Whether keratotic OLP better responds to topical retinoids than erosive OLP is still an open question that deserves further comparative and controlled clinical trials. The benefits and harms of using topical retinoids in people with OLP require thorough evaluation in properly designed controlled studies [27]

Topical retinoids such as tretinoin, isotretinoin and fenretinide, with their immunomodulating properties, have been reported to be effective in OLP. Reversal of white striae can be achieved with topical retinoids, although effects may only be temporary. Systemic retinoids have been used in cases of severe lichen planus with variable degree of success. The positive effects of retinoids should be weighed against their rather significant side effects like cheilitis, elevation of serum liver enzymes and triglyceride levels and teratogenicity [28]

7] Photodynamic therapy

Photodynamic therapy (PDT) is a technique that uses a photosensitizing compound like methylene blue, activated at a specific wavelength of laser light, to destroy the targeted cell via strong oxidizers, which cause cellular damage, membrane lysis, and protein inactivation. PDT has been used with relative success in the field of oncology, notably in head and neck tumors. PDT is found to have immunomodulatory effects and may induce apoptosis in the hyperproliferating inflammatory cells which are present in psoriasis and lichen planus. This may reverse the hyperproliferation and inflammation of lichen planus. In this MB was used as photosensitizer. MB is a commercially available medical dye. It is a tricyclicphenothiazine dye. Peak absorption of MB is maximum at 652 nm. The fluorescence spectrum is centered at 683 nm. Ten minutes prior to laser irradiation, patients were instructed to gargle a MB solution in water of 5% concentration for 5 minutes. A diode laser (Lumina1,Russia; 632 nm, CW, 1 W) was used as the light source. The lesions and 0.5 cm of their surrounding marginal zone were illuminated with a spot size of 1 cm². Large lesions were illuminated with multiple spots. A light exposure dose of 120 J/cm² was used for 2 minutes results showed that MB-PDT has a quick and significant beneficial effect in the control of the main symptoms and signs of OLP with minimal adverse effects. [13]

Sobaniec et al. used chlorin e6 (Photolon) as a photosensitizer and a semiconductor laser, with power up to 300 mW and a wavelength of 660 nm to assess the clinical efficacy of photodynamic therapy in the treatment of oral lichen planus. The mean 55% reduction of lesions was obtained in the study in favor of the introduction of PDT as an alternative therapy for OLP [21].

Also Sadaksharam et al. in 2012 evaluated 20 patients with systemic OLP. PDT with xenon arc lamp of 630 ± 5 nm wavelength and total dose of 120 J/cm² in four visits and photosensitizer of MB was done. They achieved a significant reduction in lesions over prolonged period without any side effects [22]

8] PUVA therapy

Photochemotherapy with solar radiation (PUVASOL) has been introduced as an effective and cheaper alternative to PUVA. A comparative study by Sharma et al. demonstrated that PUVASOL can be used as an alternative therapy for OLP that is equally effective as or more effective than conventional OLP therapies[15]

Another study done which compared the clinical effects of photodynamic therapy to dexamethasone mouthwash in the treatment of oral lichen planus lesions. Photodynamic therapy was as effective as the dexamethasone mouth wash in the treatment of oral lichen planus. It could be used as a safe modality in the treatment of oral lichen planus lesions without identified side effects.[16]

photochemotherapy with 8-methoxypsoralen and long wave ultraviolet light (PUVA). Psoralens are compounds found in many plants, which make the skin temporarily sensitive to UV radiation. Methoxypsoralen is given orally, followed by administration of 2 hours of UV radiation intraorally in the affected sites. It has been successfully used in the treatment of severe cases of OLP.[18] Two major disadvantages of PUVA therapy include the adverse effects of nausea and dizziness secondary to psoralen and 24-hour photosensitivity when this medicine is taken orally. Also, dosimetry can be difficult within the complicated geometry of the mouth, because PUVA is usually administered on skin over large, open surfaces.[19]

9] Laser therapy

In this Er :YAG laser is used for reducing symptoms and lymphoplasmocytic infiltrate in case of oral lichen planus. The parameters used were as energy, 80–120 mJ; frequency, 6–15 Hz; non-contact hand piece; spot size diameter, 0.9 mm; pulse duration, 100 µsec (VSP) to 300 µsec (SP) ; fluences, 12.6–18.9 J/cm²; and air/water spray (ratio: 6/5). The use of this wavelength offers several advantages including, a good and fast healing process, a very low level of discomfort during and after intervention, and a rapid disappearance of symptoms. further studies and long-term follow-up will be necessary.[14]

ajarm et al. also demonstrated that Low Intensity Laser Therapy was as effective as topical corticosteroid therapy without any adverse effects and it could be considered as an alternative treatment for erosive-atrophic OLP. Their research which was done on thirty patients with erosive-atrophic OLP .One group consisted of patients treated with the 630 nm diode laser and the other group received Dexamethasone mouth wash. Appearance score, pain score, and lesion severity was reduced in both groups. No significant differences were found between the treatment groups regarding the response rate and relapse.[23]

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