



The Diagnosis and Management of Oral Lichen Planus: a Consensus Approach

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Summary: Lichen planus (LP) is a common oral disorder, reviewed at an international meeting between the American Academy of Oral Medicine (AAOM) and International Federation of Oral Medicine (IFOM) in Montreal, Canada in 2001. This paper is a summary of the proceedings of that meeting.

Oral LP is of uncertain etiopathogenesis. Diagnosis is mainly on clinical grounds. Since there is still no conclusive evidence relevant to the etiology, therapy has traditionally attempted to suppress symptoms rather than to address the basic issues of susceptibility and prevention.

Conclusions: Symptomatic relief can be achieved in the majority of patients with topical corticosteroids alone, or other immunomodulatory topical agents, or combinations. Only infrequently do patients require the prolonged use of intralesional or systemic medications to control the disease process.

Key words: lichen planus, oral, etiopathogenesis, diagnosis

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INTRODUCTION

Lichen planus (LP) is a common chronic oral inflammatory disease, which can affect skin, nails, scalp and other mucosae. The prevalence is between 0.1 and 4 percent (Axell and Rundquist, 1987; Bouquot and Gorlin, 1986). LP is most frequent in the 40 to 70 years age range (Salem, 1989), and females predominate in a proportion of about two-to-one (Silverman et al, 1985; Thorn et al, 1988).

Etiopathogenesis

LP may represent a type IV hypersensitivity response to an antigen that could have altered keratinocyte function (Porter et al, 1997). It is a clinical and histological reaction to a variety of heterologous stimuli (Eversole, 1997). There is a cell-mediated immune response to epithelial-associated antigen, and the submucosal leukocyte population is predominantly T lymphocytic (Toto and Nadimi, 1987) with both CD4- and CD8-positive cells submucosally, and CD8 cells in the epithelium (Toto and Nadimi, 1987). T cells migrate to the oral epithelium

mediated by adhesion molecules (ICAM-1 and VCAM). Upregulation of ELAM-1, ICAM-1, and VCAM-1 (especially by endothelial cells in the subepithelial vascular plexus) could play a role in the pathogenesis of LP (Regezi et al, 1996). Chemokines (Sugerman et al, 1996) (IL-1, -8, -10, -12 and TNF), secreted by keratinocytes are chemotactic for lymphocytes. Tumor necrosis factor-alpha (TNF-alpha), a cytokine involved primarily in T-cell-mediated immunopathological reactions, is implicated since it is found in diseases which bear clinical and histological similarities to LP (Simark-Mattsson et al, 1999).

In addition, there is upregulation of epithelial basement membrane extracellular matrix (ECM) proteins, including collagen types IV and VII, laminin and certain integrins – serving as pathways for T cell migration (Eversole, 1997). T cells then bind to keratinocytes and programmed cell death (apoptosis) is implicated in the basal cell destruction of LP (Dekker et al; Bloor et al, 1999; Majorana et al, 1999; Tanda et al, 2000).

Genetic background: familial LP is rare, and no studies have shown significant association with any particular

HLA antigen (Mahood, 1983; Grunnet and Schmidt, 1983).

Infectious agents: an infective role remains speculative (Scully et al, 1998).

Liver disease: there is an association of LP and HCV in southern Europe and in Japan (Dupin et al, 1997; Bagan et al, 1998; Ingafou et al, 1998; Lodi et al, 1997; Arrieta et al, 2000; Carozzo et al, 1999; del Olmo et al, 2000; Grote et al, 1998; Grote et al, 1999; Kirby et al, 1998; Lodi et al, 2000; Mignogna et al, 1998; Mignogna et al, 2000; Nagao et al, 1998; Nagao et al, 1999; Nagao et al, 2000b; Nagao et al, 2000a; Roy et al, 2000; van der Meij and van der Waal, 2000; Varela et al, 2000). No logical explanation for this has been established and no such association is seen in British (Ingafou et al, 1998), German (Grote et al, 1999), Irish (Roy et al, 2000), or Dutch (van der Meij and van der Waal, 2000) patients.

Stress: it has not been established whether the observed psychological alterations constitute a direct etiologic factor, or whether such alterations are a consequence of the disease (Rojo-Moreno et al, 1998).

Clinical Features

Lichen planus often affects the oral mucosa, and lesions can occur without skin lesions; 20% of patients with oral lesions also have extraoral lesions (Silverman et al, 1985), while approximately 50% of patients with skin lesions also have oral LP. Eisen (1999) found extraoral manifestations included cutaneous LP in 16% of patients, genital LP in 19% of women and 4.6% of men. Oral LP is most common in the buccal mucosa, tongue and gingiva; and usually bilateral. Andreasen (1968) recognised reticular, papular, atrophic, ulcerative or erosive, plaque-like and bullous forms. Others distinguish three groups: reticular, atrophic and erosive (Silverman et al, 1985; Lozada-Nur and Miranda, 1997a). The ulcerative form is most likely to cause symptoms, from spontaneous soreness to severe pain accentuated by local irritants and trauma. Atrophic forms are quite common on the gingivae, constituting one form of desquamative gingivitis (Scully and Porter, 1997).

Lichenoid Reactions

Lichenoid reactions (LR) are lesions with an identifiable etiology but clinically and histologically so similar to LP that, in many cases, differentiation is difficult or impossible (McCartan and McCreary, 1997).

Dental Materials

In a few cases contact with amalgam can cause lichenoid reactions (Yiannias et al, 2000; Koch and Bahmer, 1999; Cederbrant et al, 1999; Camisa et al, 1999; Ostman et al, 1996; Bratel et al, 1996), and occasionally the lesions improve after substitution by some other restorative material (Bratel et al, 1996).

Lichenoid Drug Reactions (LDR)

Drugs reported to cause lichenoid reactions include non-steroidal anti-inflammatory drugs (NSAIDs), the angiotensin-converting enzyme inhibitors (ACEIs), anti-malarials and gold (McCartan and McCreary, 1997).

Diagnosis

The diagnosis of oral LP should not be based solely on the clinical aspects since it can mimic disorders such as keratoses, lupus erythematosus and even carcinoma. A histological diagnosis is therefore essential, the histopathological criteria being (Andreasen, 1968):

- Hyperortho- or hyperparakeratosis in reticular lesions, and epithelial thinning in atrophic clinical lesions. In the erosive form, the epithelium becomes detached, leaving an exposed connective tissue surface
- Degenerative changes of the basal cells
- A band-like subepithelial infiltrate of lymphocytes and histiocytes.

However, the histopathological assessment, based on the available WHO definition, is rather subjective and insufficiently reproducible (van der Meij and van der Waal, 2003) and stricter diagnostic criteria are required. Immunofluorescence studies may be helpful. Direct immunofluorescence (IFD) shows the basal lamina staining positively for fibrinogen – a protein not normally seen there. Immunofluorescence projects downwards into the submucosa, producing a stalactite appearance (Eversole, 1997; Schiodt et al, 1981; Gombos et al, 1992; Okochi et al, 1990; Hintner et al, 1990).

Using indirect immunofluorescence (IIF), a subpopulation of patients has been shown to have circulating antibodies that bind to cytoplasm of basal keratinocytes. This phenomenon was said to be more prevalent in lichenoid drug reactions (Lamey et al, 1995) but the same workers reported that lichen planus-specific antigen is not a useful marker to distinguish oral lichenoid drug eruptions from idiopathic LP (McCartan and Lamey, 2000).

The identification of lichenoid reactions is difficult. Unilateral lesions (Lamey et al, 1995) with erosive com-

ponents have been reported to be more frequently lichenoid (Potts et al, 1987) though this is not always the case. Histologically, lichenoid drug reactions exhibit a more diffuse lymphocytic infiltrate, with eosinophils and plasma cells, and there may be more colloid bodies than in idiopathic oral LP. However, those findings are also not diagnostic. The most reliable diagnostic feature of lichenoid reactions is that they remit on withdrawal and reappear on rechallenge (Scully et al, 1998).

Management

The possibility that the lesions may be lichenoid reactions should be considered before initiating therapy (Bolewska et al, 1990). When identified, such lesions can sometimes show considerable improvement after replacement of the offending restorations (Finne et al, 1982) or drug (Potts et al, 1987; Robertson and Wray, 1992).

Exacerbating Factors

The Koebner phenomenon, whereby lesions develop in response to trauma, is common in LP (Eisen, 1993b). Thus, eliminating or correcting causative factors such as sharp or rough dental restorations, fractured teeth, poorly fitting dental appliances and oral habits such as cheek biting may be beneficial. The institution of an optimal oral hygiene program which eliminates dental plaque and calculus can also improve gingival LP (Holmstrup et al, 1990).

Drug Treatments

Patients with oral LP are managed with medications that were neither developed nor intended for oral diseases and, consequently, most lack adequate efficacy studies. Thus such factors as optimal dose, duration of treatment, safety, and true efficacy remain unknown (Scully et al, 2000).

Bioadhesive gels such as cyanoacrylate and hydroxy ethylcellulose, and bioadhesive polymers such as chitosan have been utilized in the oral cavity as mechanical barriers that provide pain relief from oral ulcerations including those of oral LP. Additionally, when combined with topical corticosteroids, these agents have been employed as a method of improving the local delivery of these drugs by increasing their retention at the application site, increasing drug penetration, and increasing patient acceptability. Although frequently employed in practice, a controlled study suggests that topical steroids in adhesive bases are no more effective than the base preparations (Voute et al, 1993).

A variety of topical preparations and mouthwashes have been utilized to ameliorate the pain from oral erosive diseases. Various formulations containing one or more active ingredients, including anaesthetics, antimicrobials, wound cleansers, coating agents and occlusive dressings, are widely available. Although many of these products, as claimed, reduce the pain, their benefits are modest and short in duration.

Corticosteroids

The most commonly employed and useful agents for the treatment of LP are topical corticosteroids (Table 1). Studies utilizing midpotency and superpotent corticosteroids have demonstrated the efficacy of these in 30%-75% of patients (Carrozzo and Gandolfo, 1999; Lozada-Nur and Miranda, 1997b).

Therapy should be initiated with a potent preparation to achieve a rapid response. It is advisable to lower the strength of the preparation as soon as erosions re-epithelialize and erythematous lesions become asymptomatic.

Once the disease becomes inactive i.e. absence of lesions, or presence of only white reticular lesions, therapy may be temporarily discontinued.

Patients should be warned about the off-label use of topical corticosteroids and the accompanying package inserts which state for 'external use only'. Although a number of studies have demonstrated the safety of topical corticosteroids when applied to mucous membranes for short intervals (Plemons et al, 1990; Lehner and Lyne, 1969), the potential for adrenal suppression with prolonged use necessitates careful and frequent follow-up. Furthermore, as many as one third of LP patients treated with topical corticosteroids develop secondary candidiasis (Vincent et al, 1990).

For intractable erosive LP lesions, intralesional steroids such as triamcinolone acetonide (10-20 mg/ml) injections can be highly effective and repeated every 2-4 weeks (Table 2). Other steroids such as hydrocortisone may also be used but there are no studies to suggest which steroid is preferable. Frequent injections of steroids, however, may result in an unwanted systemic dose.

Systemic corticosteroids should be reserved for recalcitrant severe erosive or erythematous LP, where topical approaches have failed, or for widespread oral LP with concomitant skin, genital, esophageal, or scalp involvement, and should only be administered by a Specialist. Daily doses of prednisone in the range of 40-80 mg are usually sufficient to achieve a response without the need for higher doses as in other mucocutaneous diseases such as pemphigus or pemphigoid. The toxicity of prednisone requires that it be used only when

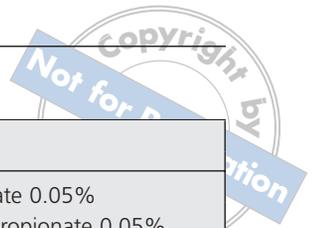


Table 1 Suggested topical corticosteroids for control of OLP

<i>Medium Potency</i>	<i>High Potency</i>	<i>Super Potency</i>
triamcinolone acetonide 0.1%	fluocinonide 0.05%	clobetasol propionate 0.05%
fluocinolone acetonide 0.025%	desoximetasone 0.25%	betamethasone dipropionate 0.05%
betamethasone valerate 0.1%	halcinonide 0.01%	halobetasol propionate 0.05%

Table 2 Some topical and systemic treatment options for OLP patients

Drug	Route	Potential Adverse Effects
Corticosteroids	Topical	Secondary candidiasis, systemic absorption, tachyphylaxis
Corticosteroids	Intralesional	Systemic absorption, pain, atrophy
Corticosteroids	Systemic	Cushing’s syndrome and suppression of the hypothalamic-pituitary-adrenal axis
Retinoids	Topical	Irritation, burning, teratogenic, photosensitivity, pigmentary changes
Retinoids	Systemic	Erosions may worsen, rashes, teratogenic, cheilitis, dermatitis, photosensitivity, myalgias, intracranial hypertension, blood chemistry and lipid level abnormalities
Hydroxychloroquine	Systemic	Ocular toxicity, gastrointestinal, complete blood count abnormalities
Ciclosporin	Topical	Burning, accumulation of waxy particles, systemic absorption and nephrotoxicity
Ciclosporin	Systemic	Bone marrow suppression, increase risk of infection and malignancy, hepatic and renal damage, numerous other adverse effects
Azathioprine	Systemic	
Mycophenolate	Systemic	
Tacrolimus	Topical	Stinging. Systemic absorption and nephrotoxicity

necessary, at the lowest dose possible and for the shortest duration of time. Therefore, prednisone should either be administered for very brief periods of time i.e. less than 5-7 days and then abruptly withdrawn, or the dose should be reduced by 5-10mg/day gradually over a 2-4 week period. If patients are able to tolerate alternate day administration of the same total dose, adverse effects may be minimized.

Additional Topical Treatment Options

The topical use of cyclosporine (ciclosporin) may be used as an adjunct to topical corticosteroids (Eisen et al, 1990; Harpenau et al, 1995). The standard solution (100 mg/ml) intended for systemic use in organ transplant recipients may be used as a mouthrinse in oral LP. The solution is prohibitively expensive for routine use and should be reserved for patients who are symptomatic. Topical retinoids such as tretinoin have been reported to be effective for oral LP (Sloberg et al, 1979). Retinoids applied to the skin often cause con-

siderable irritation and inflammation, and the same is to be expected when applied to oral mucous membranes. Cheilitis is common.

Additional Systemic Treatment Options

None of the systemic drugs used for LP result in long-term remission and the disease usually recurs when they are withdrawn. Nevertheless, despite these shortcomings, systemic agents usually generate significantly better results than topical agents alone. A range of systemic agents may be employed for the treatment of oral LP in patients who are unresponsive to topical agents. All these drugs require monitoring for laboratory abnormalities and should be administered only by specialists familiar with their adverse effects.

Hydroxychloroquine may be used to control LP at daily doses of 200-400 mg (Eisen, 1993a). The systemic retinoids, acitretin (Laurberg et al, 1991), and isotretinoin (Camisa et al, 1999) can be beneficial when administered to patients with erosive LP. Several immuno-

suppressive agents can be employed for severe LP including azathioprine (100-150 mg/day), ciclosporin (2-4 mg/kg/day) and mycophenolate (2-3 gm/day).

A list of treatment options and adverse effects is summarized in Table 2, including topical immunosuppressives, introduced subsequent to this symposium. Tacrolimus, a steroid-free topical immunomodulator specifically developed as treatment for atopic dermatitis, has been reported to benefit patients with erosive LP, and has a good safety record (Vente et al, 1999; Olivier et al, 2002; Morrison et al, 2002; Rozycki et al, 2002; Kaliakatsou et al, 2002). Pimecrolimus, a similar agent, also shows promise (Ling, 2001).

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