Oral Lichen Planus – Known and Unknown: a Review

Maria Z. Mutafchieva1, Milena N. Draganova-Filipova2,3, Plamen I. Zagorchev4, George T. Tomov1

1 Department of Periodontology and Oral Diseases, Faculty of Dental Medicine, Medical University of Plovdiv, Plovdiv, Bulgaria
2 Department of Medical Biology, Faculty of Medicine, Medical University of Plovdiv, Plovdiv, Bulgaria
3 Technological Center of Emergency, Plovdiv, Bulgaria
4 Department of Medical Physics and Biophysics, Faculty of Pharmacy, Medical University of Plovdiv, Plovdiv, Bulgaria

Correspondence: Maria Z. Mutafchieva, Department of Periodontology and Oral Diseases, Faculty of Dental Medicine, Medical University of Plovdiv, 3 Hristo Botev Blvd., 4000 Plovdiv, Bulgaria
E-mail: maria_mwow@abv.bg
Tel: 00359883339644

Received: 14 Jun 2017
Accepted: 04 Feb 2018
Published online: 26 Feb 2018
Published: 29 Nov 2018

Key words: OLP, etiology, pathogenesis, diagnosis, treatment, malignant potential

Citation: Mutafchieva MZ, Draganova-Filipova MN, Zagorchev PI, Tomov GT. Oral lichen planus – known and unknown: a review. Folia Med (Plovdiv) 2018;60(4):528-35. doi: 10.2478/folmed-2018-0017

Lichen planus is a chronic mucocutaneous inflammatory disease affecting 1-2% of the general population with maximum prevalence of the disease in women above the age of 40. Its aetiology remains unclear and the pathogenesis is still the object of much speculation. It is considered to be an autoimmune disorder mediated mainly by the T-lymphocytes. The present paper presents the most well-known external agents (viruses in particular), internal agents like stress, and the heat shock protein thought to be trigger factors and describes the action of different cells and proteins associated with the development of that disease. Diagnosis is based on clinical and histopathologic evidence; direct and indirect immunofluorescence techniques can also be of use. Despite the wide variety of therapeutic modalities, treatment outcomes are often insufficient. Currently, topical corticosteroids are widely accepted as a standard therapy, but also retinoids, calcineurin inhibitors and other immunosuppressants can be administered. Because of the aspect relevant to these drugs, priority is given to alternative harmless methods such as LLLT and PDLT. There is an ongoing controversy in the literature about the possible premalignant character of oral lichen planus, however, periodic follow-up is recommended.

INTRODUCTION

Lichen planus (LP) is a chronic inflammatory mucocutaneous disease of unknown etiology.1,2 Oral lesions often precede skin lesions, and in many cases they remain the only manifestation of the disease. Nasal, laryngeal, esophageal, genital or anal mucosa may also be affected.2,3 In rare cases, the disease can present with lesions on the scalp or nails.3,4

Oral lichen planus (OLP) is a relatively common disease affecting between 0.5% and 2.2% of the population; the ratio of males to females is 1:2.5 People in the age range of 30 to 60 years are affected.3,6 There are few reports on LP occurring in childhood.2,7

OLP can affect all parts of the oral cavity. The most common location is the buccal mucosa, followed by the lingual, gingival and labial mucosa.2,4 Bilateral symmetrical distribution of the lesions predominantly occupying posterior regions of the mouth is typical of this disease. The Andreasen classification system distinguishes six clinical forms of OLP: reticular, papular, plaque-like, atrophic (erythematous), erosive-ulcerous and bullous-erosive.1,2,4,7-9 Reticular, papular and plaque-like forms are usually painless and present clinically as white keratotic lesions. In the atrophic, erosive and bullous forms, symptoms range from mild discomfort to episodes of intense pain.1,2,7,8 A pathognomonic sign of this disease is the presence of the so-called Wickham striae - white hyperkeratotic papules (striae), giving lace-like appearance of the lesions. OLP can manifest in the form of desquamative gingivitis.4 This oral presentation is part of the symptom group of the so called vulvo-vaginal-gingival syndrome which includes the triad of LP of vulvar, vaginal and gingival mucosa.10 A routine examination by a specialist is recommended for female patients with OLP, even in the absence of...
Oral lichen planus – known and unknown

Oral lichen planus is characterized by alternating periods of remissions and exacerbations. The condition can be triggered by psychological or physical stress, the presence of chronic mechanical trauma, consumption of irritating foods and beverages.

**Etiology**

The etiology of OLP is still unknown. Existence of an antigen capable of changing antigen specificity of basal keratinocytes, thus making them target for the cell-mediated immunity, is under discussion. This triggering factor can be of external or internal origin.

**Factors of external origin**

- **Viruses**
  
  Hepatitis C virus (HCV) has been extensively investigated as a possible etiological factor of OLP. Recent meta analysis on that topic demonstrated a positive correlation between HCV and LP. This association can be explained by the ability of the virus to replicate in non-hepatocyte cell types, such as skin and oral mucosa cells. On the other hand, the high variability of the virus, resulting in a continuous reactivation of immune cells, increases the risk of development of autoimmune diseases. However, it should be noted that modern therapy of patients with chronic liver disease includes interferon-gamma and ribavirin - drugs often considered as a cause for triggering lichenoid reactions.

  In a meta-analysis, Syrjänen et al. found a strong association between HPV and oral squamous cell cancer and other premalignant conditions. The levels of HPV 16 were statistically higher in patients with OLP compared to healthy controls. These data suggest that HPV may play a role both in the etiology and in malignant transformation of lichen planus. On the other hand, the detection of HPV DNA in OLP lesions can be explained by the presence of ulcerated areas vulnerable to viral invasion, as well as by immunosuppressive corticosteroid therapy administered in these patients which facilitates viral replication.

  Possible association between OLP and Epstein-Barr virus, herpes simplex, cytomegalovirus, etc., is under discussion.

- **Factors causing lichenoid reactions (LR)**
  
  Potential exogenous factors may be some medications and dental restorative materials. In these cases, lesions clinically and histologically similar to those in OLP are observed, and they are referred to as lichenoid reactions. Unlike idiopathic LP, in these conditions there is a specific causative factor, the removal of which leads to regression of lesions. Contact LR, drug-induced LR and LR associated with graft-versus-host disease can be differentiated.

  **Contact lichenoid reactions** occur most often near mercury-containing amalgam fillings, and they are manifestation of the delayed-type hypersensitivity. More rarely, a triggering factor may be other restorative materials such as gold, porcelain, acrylic plastics, resins, glass-ionomer cements, etc.

  Medications that may induce lichenoid reactions include: antihypertensive drugs – ACE-inhibitors, β-blockers; NSAIDs; antimalarial drugs; oral hypoglycemic agents; gold salts and penicillamine, used for the treatment of rheumatoid arthritis.

  Lichenoid reactions may also occur in patients who have undergone stem cell transplantation or bone marrow transplantation as part of the symptom group of graft-versus-host disease (GVHD). The concomitant immunosuppressive therapy increases the risk of developing neoplasia, defining this type of LR as lesions with high malignant potential.

**Factors of internal origin**

- **Psychological disorders**
  
  Recent studies show the association between mental stressors and the occurrence and progression of chronic diseases. Neuroendocrine hormones released during stress exposure cause disturbance of the balance between Th1 and Th2 cytokines, which is associated with the development of autoimmune diseases. A high percentage of patients with LP have reported onset of the disease and exacerbations at the time of increased emotional stress. Shah B et al. found statistically higher levels of stress, depression and anxiety, correlating with elevated levels of cortisol in saliva in patients with OLP compared to healthy individuals. In contrast, in a study conducted by Girardi C et al., the stress, depression, and anxiety levels and salivary cortisol and dehydroepiandrosterone (DHEA) levels in patients with the OLP did not differ from those in the control group.

- **Heat shock proteins**
  
  High levels of expression of heat shock proteins (HSPs) found in OLP lesions determine their potential role of autoantigens in the pathogenesis of the disease. It is assumed that dysregulation of the gene responsible for the expression of these
proteins in the epithelial cells and its inability to suppress the immune response result in recognition of body’s own HSPs as foreign substances. On the other hand, the natural increase in these proteins as a result of external factors such as temperature changes, UV light, drugs, viruses, etc., raises the question whether HSPs are the primary etiological factor for the disease or their increase is a consequence of another factor of external origin.

- **Genetic factors**

Research focused on the possible genetic predisposition to the disease demonstrated an association between HLA-DR1 and idiopathic cutaneous lichen, as well as the association between HLA-DR6 and hepatitis C related OLP. A case of OLP simultaneously affecting a five-member Chinese family was reported suggesting the presence of a hereditary predisposition due to a mutation in 3p14-3q13 chromosome. However, the evidence in literature is insufficient to conclude that the disease is genetically determined.

**Pathogenesis**

The pathogenesis of this disease is a subject of various hypotheses. OLP is a chronic inflammatory disease in which the CD8+ T cells induce apoptosis of basal keratinocytes. These mechanisms are triggered by expression of the putative antigen on the surface of keratinocytes at the early stages or by recognizing the body’s own peptides as foreign antigens. Various cell types - keratinocytes, Langerhans cells (LC), CD4+, CD8+ T-Ly, macrophages and mast cells, cytokines and chemokines secreted by them, and proteins of the extracellular matrix are involved in triggering the disease by activation of various pathogenic pathways. Four main mechanisms have been described.

The sequence of cell-mediated immune response is as follows: migration of T-Ly in the epithelium, their activation and then “killing” the keratinocytes. Lymphocytes are attracted by chemokines secreted by Ag-modified keratinocytes. Activation of migrated CD8+ Tc may be direct, through detection of the antigen expressed by the keratinocytes by MHC class I molecules, or indirect through initial activation of CD4+ cells. The Langerhans cells play a major role in the latter where they present the responsible antigen to the helper cells via MHC class II molecules which in turn activate CD8+ Tc via RCA-receptor or through secretion of IL-2, IFN-γ, TNF-α. In the final stage of the immune response, activated CD8+ Tc destroy basal keratinocytes through TNF-α, Fas-FasL or granzyme B-mediated apoptosis.

**Nonspecific immune response** includes mechanisms triggered as a result of the destruction of the basement membrane (BM), activation of matrix metalloproteinases (MMPs), secretion of chemokines, mast cell degranulation, etc.

Keratinocytes secrete type IV collagen and laminin 5, which maintain basement membrane integrity, which in turn releases signals suppressing apoptosis in epithelial cells. After basal keratinocytes are damaged, BM is impaired and it loses its ability to inhibit apoptosis and attracts non-specific T-Ly to the affected areas.

The expression levels of MMPs, especially MMP-9, in OLP lesions are significantly higher than those in healthy controls. MMP-9 induces BM destruction, thus fulfilling a non-specific role in the pathogenesis of the disease.

**Chemokines.** RANTES is a proinflammatory cytokine secreted by activated lymphocytes, keratinocytes, and numerous other cells. Its effect results in degranulation of mast cells, which in turn triggers the release of TNF-α and chymase. TNF-α stimulates the release of lymphocytes in the extravasal region. After activation, they secrete RANTES again. Thus a vicious cycle is established, responsible for the chronic course of the disease.

60% of mast cells in OLP lesions are found degranulated. This is accompanied by the release of a series of cytokines - IL-3, IL-4, IL-5, IL-6, IL-8, IL-10, IL-13 and IL-16, TNF-α, chymase and RANTES. Chymase is a protein capable of inducing the production of MMP-9 by lymphocytes, thus demonstrating the indirect role of mast cells in the destruction of BM.

**Autoimmune hypothesis** is supported by a number of characteristics of the disease: chronic course; manifestation in adults; predominantly affecting the female gender; presence of T-lymphocytes in the lesion; other autoimmune comorbidities; efficacy of immunosuppressive therapy.

TGF-β1 suppresses immune response to self-antigens and its deficiency predisposes the body to the development of autoimmune diseases. Low expression of this growth factor in OLP lesions is reported.

Heat shock proteins are considered as potential autoantigens. Their higher expression of keratinocytes in the affected areas is another indication of the involvement of autoimmunity in the pathogenesis of the disease.
According to Langerhans-mediated autoimmune hypothesis, autoantigens are the apoptotic keratinocytes themselves. After their phagocytosis, LC activate Th, and they in turn - CD8+ Tc, thereby enhancing cell death. 1, 21

Evidence from different authors has suggested the involvement of humoral immunity in the pathogenesis of the disease due to circulating autoantibodies against desmogleins 1 and 3 22 and anti-basal cell antibodies 23 they detected in the serum of patients with OLP.

**DIAGNOSIS**

- **Histology**

OLP histological definition was given by the WHO in 1978 in ‘A Coded compendium of the International Histological Classification of Tumours’. The following criteria are listed: hyperkeratosis (ortho- or parakeratotic type), acanthosis or epithelial atrophy, liquefaction of basal keratinocytes, dense band-like lymphocytic infiltrate in the superficial lamina propria. Epithelial rete ridges are often missing or may have a ‘saw teeth’ appearance. 9 Amorphous eosinophilic deposits - civatte bodies - are found in the basal cell layer and the superficial lamina propria, being degenerate keratinocytes. 1, 3, 9

The histological characteristics of lichen planus are typical, but non-specific. Onofre et al. found clinicopathological discrepancies in the diagnosis of OLP in a quarter of the selected cases. 24 Based on these results van der Waal concluded that an accurate diagnosis can be made only by subtle interpretation of the results from both clinical and histological examination, and introduced a set of modified diagnostic criteria for OLP. 25

- **Direct immunofluorescence (DIF)**

The most characteristic feature in immunofluorescence examination of biopsy material from patients with OLP is the detection of fibrinogen in the form of linear or granular deposits, either alone or in combination with other immunoreactants along the basal membrane and/or the superficial lamina propria. 3, 7 The changes in this type of study are also non-specific, and the observed immunological deposits vary between authors. 26, 27 Arora et al. report that detecting immunofluorescent civatte bodies (CB) is among the most important characteristics in DIF of patients with lichen planus along with fibrinogen deposits. 3

- **Indirect immunofluorescence (IIF)**

Using IIF, Lin SC et al. detected anti-basal cell antibodies in the serum of 54% of the 63 patients with OLP they examined. 23

Although non-specific, immunofluorescence assay can be used as an auxiliary tool to diagnose clinically and histologically atypical cases of LP. DIF and IIF are obligatory in patients with bullos form of OLP and manifestation in the form of desquamative gingivitis in order to distinguish it from pemphigus vulgaris, MMP, dermatitis herpetiformis and others.

**TREATMENT**

Given the unclear etiology of OLP, the results of administering agents for its treatment are often unsatisfactory. Treatment is aimed primarily at abolishing the symptoms and at extending the periods of remission. At this stage, complete eradication of the disease cannot be achieved by any method. 21

It is essential to eliminate local irritating or aggravating factors in the oral cavity (sharp edges of fillings, fractured teeth, harmful habits). Scaling and instructions for optimum oral hygiene improve the condition in patients with gingival LP. 4, 6, 21 Diet that excludes irritating foods and drinks, smoking and alcohol consumption is recommended. Patients with reticular form or other asymptomatic OLP lesions do not need any other treatment. 21 Three groups of therapeutic modalities are distinguished: drug therapy, surgery and phototherapy.

- **Drug therapy**

Among the pharmacological treatments of OLP, four main groups are administered with varying degrees of utility: corticosteroids, retinoids, calcineurin inhibitors and other immunosuppressants. Priority shall be given to topical drug therapy because of fewer adverse effects. Systemic medication is administered in the event of widespread erosive areas, as well as in simultaneous involvement of oral cavity, skin and/or other mucous membranes. 4, 21

Corticosteroids (CSs) are used as first line therapy. Administration can be topical, intralesional or systemic. 4 Topical forms are most widely used. The efficiency of this type of therapy in patients with OLP ranging between 30-75% for moderately and highly efficient CSs 4, and 56-75% for clobetasol propionate 21. Local administration of this group of medications poses a risk of development of oral candidiasis and/or tachyphylaxis. 3, 21, 28

Intralesional injections of triamcinolone acetonide showed good results in erosive forms of OLP refractory to treatment. This type of application is painful and carries the risk of atrophy of the
treated areas and of adverse systemic absorption of the medication.4

Most side effects were observed during prolonged treatment with systemic CS, including development of Cushing’s syndrome, hypertension, diabetes, gastric ulcers; suppression of hypothalamic-pituitary-adrenal axis; immune suppression; fungal infections, etc. Therefore, they should be administered only as indicated, in compliance with established regimens for reducing adverse drug reactions.4,6,21

Al-Hashimi et al. concluded that retinoids used for the treatment of OLP effect the clinical presentation of the disease, but show worse results than traditional corticosteroid therapy. Based on a histopathologic follow-up study, reticular OLP responded better to the treatment with retinoids than less keratinized lesions.6 Topical forms can cause transitory burning sensation or transient pigmentation in the oral cavity. Systemic administration of vitamin A is associated with a number of serious side effects - increase in transaminase levels, hyperlipidemia, rash or photosensitivity, cheilitis, alopecia, nail dystrophy, etc.4,6 Retinoids are teratogenic and therefore contraindicated in women of childbearing age.4,6

From the group of calcineurin inhibitors, cyclosporine and tacrolimus are used.

The adverse effects of topical administration of cyclosporine are minimal. Despite the significant improvement in oral symptoms, results of rinsing with cyclosporine solution are not significantly superior than those obtained when administering triamcinolone paste.29

Studies investigating the effectiveness of 0.1% tacrolimus in patients with symptomatic OLP refractory to conventional CS therapy, found a favourable therapeutic response with no serious adverse effects.30,31 Ability of tacrolimus to induce apoptosis in T-cells with simultaneous inhibition of apoptosis in non-lymphoid cells was reported.32 This mechanism of action implies reversal of the main pathological processes in the pathogenesis of LP. On the other hand, the suppression of the immune system increases the risk of malignancies. Becker et al. reported a case of diagnosing squamous cell carcinoma of the tongue after a 3-year period of use of 0.1% tacrolimus ointment in a patient with OLP.32

In cases of gingival LP, the so-called occlusal therapy, in which the drug is administered locally by individual silicone splints or acrylic labial veneers, is applied successfully. This method avoids the main drawback of topical drug treatment - the inability to provide continuous contact between the agent and the treated areas.21,33

Further systemic treatment with immunosuppressants such as chloroquine and hydroxychloroquine, azathioprine, or cyclosporin is indicated in cases of severe forms of OLP, refractory to topical treatment. Their use is associated with serious adverse effects - bone marrow aplasia; immune suppression; increased risk of infections and malignancies; oto-, nephro- and hepatotoxicity.4,6 Systemic treatment achieve better results than this with topical agents, but permanent remission of the disease could not be achieved either.4

Some authors suggest the inclusion of psychiatric medication to the routine therapy of OLP, based on the high percentage of mental disorders found among this patients.2

• Conventional Surgery
Excision of pathologically changed areas is indicated in lesions with limited dimensions, as well as in all cases of histologically confirmed dysplasia. Wide excision in a disseminated form of OLP carries the risk of postoperative scarring impairing the function.

• Phototherapy
Oral administration of 8-methoxypsoralen followed by UVA (PUVA) irradiation has a positive effect on severe and refractory to treatment OLP.34 Because of its oncogenic potential PUV A therapy was replaced by safer methods of light treatment.6,28

Narrowband UVB therapy (NB-UVB 311-313 nm) is efficient, and probably with less malignant potential than PUVA.35 Kassem et al. achieved positive effect on the clinical presentation of erosive OLP, using UVB therapy.36

Phototherapy group also includes treatment using various types of lasers. In patients with OLP, laser-assisted surgery (laser ablation and laser excision) and laser biomodulation (low level laser therapy - LLLT and photodynamic laser therapy - PDLT) may be applied.

The use of laser ablation in the treatment of OLP is based on the fact that the activator of the immune aggression is located intraepithelially and the removal of tunica epithelialis in order to eliminate the causal factor results in discontinuation of the self-sustaining autoimmune process. Pakfetrat et al. used CO2 laser ablation in refractory erosive-atrophic forms of OLP and reported reduction in size - up to complete regression of lesions, and transition of erosive areas to less risky forms - atrophic or
reticular.37 Rapid symptomatic relief and efficient elimination of oral lesions with reduction in the incidence of relapses were reported after ablation using Er:YAG laser38 and diode laser (810 nm)39.

A promising method for the treatment of symptomatic OLP is the so called laser biomodulation. Low intensity laser radiation has been demonstrated to have analgesic, anti-inflammatory, regenerative and other effects.40 A series of studies reported positive results in cases of OLP refractory to medication treatment after administration of ultraviolet41,42, KTP laser (532 nm)43; red - 630 nm44, and infrared lasers - 830 nm45; 904 nm46. The efficacy of LLLT depends on a number of parameters such as wavelength, power, intensity, exposure time, number and sequence of sessions, and therefore is still controversial.

The administration of low intensity laser radiation after prior local or systemic application of photoattractant is referred to as photodynamic laser therapy. There is evidence of immunomodulating effect of this type of therapy and the ability to induce apoptosis in hyperproliferating inflammatory cells.5,28 PDLT demonstrates consistent improvement in clinical presentation of OLP without any adverse effects, regardless of the type of photoattractant used: methylene blue5, photolon 47 or porphyrin28.

MALIGNANT POTENTIAL

In 2005, the WHO classified OLP as a potentially malignant condition.1 Transformation to squamous cell carcinoma was observed in 0.5-2% of cases.1,48 Most literature sources point erosive and atrophic forms as carrying the highest risk.1,2,40 A recent meta-analysis on the topic demonstrated that regarding the potential for conversion into oral cancer, various forms of OLP have almost the same percentage distribution.48 Therefore, timely diagnosis and regular follow-up of patients with OLP are vital.

CONCLUSION

Regardless of the conducted numerous studies, the etiology and pathogenesis of LP are still unknown. The therapy administered is often unsuccessful and is associated with a number of adverse effects. The potential for malignant transformation of OLP is also contradictory. Scientific interest is focused on finding correlations with the expression of proteins regulating cell proliferation and apoptosis, and relevant to the process of carcinogenesis. The change in their expression in OLP lesions can be used as an indicator for the transformation from normal to neoplastic epithelium and will allow for the early diagnosis of lesions at high risk.

REFERENCES

1. Chitturi RT, Devy AS, Nirmal RM, et al. Oral lichen planus: a review of etiopathogenesis, clinical, histological and treatment aspects. J Interdiscipl Med Dent Sci 2014;2:142.
2. Dalirsani Z, Delavarian Z, Javadzade-Bolouri A, et al. Psychiatric comorbidity and pharmacotherapy in patients with oral lichen planus. In: Uehara T, ed. Psychiatric disorders - worldwide advances. Rijeka: InTech; 2011:223-42.
3. Arora SK, Chhabra S, Saikia UN, et al. Lichen planus: a clinical and immuno-histological analysis. Indian J Dermatol 2014;59:257-61.
4. Bagan JV, Eisen D, Scully C. The diagnosis and management of oral lichen planus: a consensus approach. Oral Biosci Med 2004;1:21-7.
5. Aghahosseini F, Arbabi-Kalati F, Fashtami LA, et al. Treatment of oral lichen planus with photodynamic therapy mediated methylene blue: a case report. Med Oral Patol Oral Cir Bucal 2006;11:126-9.
6. Al-Hashimi I, Schiffer M, Lockhart PB, et al. Oral lichen planus and oral lichenoid lesions: diagnostic and therapeutic considerations. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007;103 Suppl 25:1-12.
7. Sivolella S, Berengo M, Cernusch S, et al. Diode laser treatment is effective for plaque-like lichen planus of the tongue: a case report. Lasers Med Sci 2012;27(2):521-4.
8. Payeras MR, Cherubini K, Figueiredo MA, et al. Oral lichen planus: focus on etiopathogenesis. Arch Oral Biol 2013;58:1057-69.
9. Pindborg JJ, Reichart PA, Smith CJ, et al. Histological and therapeutic considerations. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2004;103(5):843-4.
10. Wu Y, Qiao J, Fang H. Do you know this syndrome? Vulvovaginal-gingival syndrome. An Bras Dermatol 2014;89(5):843-4.
11. Lodi G, Pellicano R, Carrozzo M. Hepatitis C virus infection and lichen planus: a systematic review with meta-analysis. Oral Dis 2010;16:601-12.
12. Syrjanen S, Lodi G, von Bultzingslowen I, et al. Human papilloma viruses in oral carcinoma and oral potentially malignant disorders: a systematic review. Oral Dis 2011;17:58-72.
13. Yildirim B, Sengüven B, Demir C. Prevalence of herpes simplex, Epstein Barr and human papilloma viruses in oral lichen planus. Med Oral Patol Oral Cir Bucal 2011;16(2):170-4.
14. Sun A, Chang JG, Kao CL, et al. Human cytomega-
lovirus as a potential etiologic agent in recurrent aphthous ulcers and Behçet’s disease. J Oral Pathol Med 1996;25(5):212-8
15. Girardi C, Luz C, Cherubini K, et al. Salivary cortisol and dehydroepiandrosterone (DHEA) levels, psychological factors in patients with oral lichen planus. Arch Oral Biol 2011;56(9):864-8.
16. Shah B, Ashok L, Sujatha GP. Evaluation of salivary cortisol and psychological factors in patients with oral lichen planus. Indian J Dent Res 2009;20:288-92.
17. La Nasa G, Cottoni F, Mulargia M, et al. HLA antigen distribution in different clinical subgroups demonstrates genetic heterogeneity in lichen planus. Br J Dermatol 1995;132(6):897-900.
18. del Olmo JA, Pascual I, Bagán JV, et al. Prevalence of hepatitis C virus in patients with lichen planus of the oral cavity and chronic liver disease. Eur J Oral Sci 2000;108:378-82.
19. Wang Z, Yao H, Cui B, et al. Genetic linkage analysis of oral lichen planus in Chinese family. Genet Mol Res 2011;10(3):1427-33.
20. Lavanya N, Jayanthi P, Rao UK, et al. Oral lichen planus: an update on pathogenesis and treatment. J Oral Maxillofac Pathol 2011;15(2):127-32.
21. Córdova P, Rubio A, Echeverría P. Oral lichen planus: A look from diagnosis to treatment. J Oral Res 2011;10(3):1427-33.
22. Lukac J, Brozović S, Vucević-Boras V, et al. Serum autoantibodies to desmogleins 1 and 3 in patients with oral lichen planus. Croat Med J 2006;47(1):53-8.
23. Lin SC, Sun A, Wu YC, et al. Presence of anti-basal cell antibodies in oral lichen planus. J Am Acad Dermatol 1992;26(6):943-947.
24. Onofre MA, Sposto MR, Navarro CM, et al. Potentially malignant epithelial oral lesions: discrepancies between clinical and histological diagnosis. Oral Dis 1997;3:148-52.
25. van der Meij EH, van der Waal I. Lack of clinicopathologic correlation in the diagnosis of oral lichen planus based on the presently available diagnostic criteria and suggestions for modifications. J Oral Pathol Med 2003;32(9):507-12.
26. Aoki V, Sousa Jr JX, Fukumori LMI, et al. Direct and indirect immunofluorescence. An Bras Dermatol 2010;85(4):490-500.
27. Nangia A, Kumar V, Logani KB. An immunopathological study of lichen planus. Indian J Dermatol Venereol Leprol 2000;66:76-8.
28. Pavlic V, Vujic-Aleksic V. Phototherapy approaches in treatment of oral lichen planus. Photodermatol Photoimmunol Photomed 2014;30:15-24.
29. Sieg P, Von Domarus H, Von Zitzewitz V, et al. Topical cyclosporin in oral lichen planus: a controlled, randomized, prospective trial. Br J Dermatol 1995;132:790-4.
30. Malik U, Gupta S, Malik SD, et al. Treatment of symptomatic oral lichen planus (OLP) with 0.1% tacrolimus powder in Oraguard-B - a pilot prospective study. Saudi Dent J 2012;24(3-4):143-8.
31. Eckardt A, Völkerb B, Starkea O, et al. Topical tacrolimus in erosive oral lichen planus: an effective treatment approach. Oral Biosci Med 2005;4:235-40.
32. Becker JC, Houben R, Vetter CS, et al. The carcino-nogenic potential of tacrolimus ointment beyond immune suppression: a hypothesis creating case report. BMC Cancer 2006;6:7-13.
33. Motta ACF, Komesu MC, Grisi MFM, et al. Topical occlusive corticosteroid for the treatment of gingival manifestations of vesicobullous autoimmune diseases. An Bras Dermatol 2006;81(3):283-5.
34. Lundquist G, Forsgren H, Gajecck M, et al. Photopherotherapy of oral lichen planus. A controlled study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1995;79:554-8.
35. Tanew A, Radakovic-Fijan S, Schemper M, et al. Narrow band UV-B phototherapy vs photochemotherapy of oral lichen planus: a study. J Am Acad Dermatol 2012;66:761-6.
36. Pakfetrat A, Falaki F, Ahrafi F, et al. Removal of refractory erosive-atrophic lichen planus by the CO2 laser. Oral Health Dent Manag 2014;13(3):595-9.
37. Fornaini C, Raybaud H, Augros C, et al. New clinical approach for use of Er:YAG laser in the surgical treatment of oral lichen planus: a report of two cases. Photomed Laser Surg 2012;30(4):234-8.
38. Akbulut N, Kursun ES, Tumer MK, et al. Is the 810-nm diode laser the best choice in oral soft tissue therapy? Eur J Dent 2013;7(2):207-11.
39. Walsh LJ. The current status of low level laser therapy in dentistry. Part I. Soft tissue applications. Aus Dent J 1997;42:247-54.
40. Passeron T, Zakaria W, Ostovari N, et al. Treatment of erosive oral lichen planus by the 308 nm excimer laser. Lasers Surg Med 2004;34:205.
41. Köllner K, Wimmershoff M, Landthaler M, et al. Treatment of oral lichen planus with the 308-nm excimer laser. Lasers Surg Med 2004;34:205.
42. Köllner K, Wimmershoff M, Landthaler M, et al. Treatment of oral lichen planus by the 308 nm excimer laser – early preliminary results in eight patients. Lasers Surg Med 2003;33:158-60.
43. Fornaini C. LLLT in the symptomatic treatment of oral lichen planus. Laser Ther 2012;21(1):51-3.
44. Mahdavi O, Boostani N, Jajarm H, et al. Use of low level laser therapy for oral lichen planus: report of
two cases. J Dent (Shiraz) 2013;14(4):201-4.
45. Cafaro A, Albanese G, Arduino PG, et al. Effect of low-level laser irradiation on unresponsive oral lichen planus: early preliminary results in 13 patients. Photomed Laser Surg 2010;28(2 Suppl.):99-103.
46. Cafaro A, Arduino PG, Massolini G, et al. Clinical evaluation of the efficiency of low-level laser therapy for oral lichen planus: a prospective case series. Lasers Med Sci 2014;29(1):185-90.
47. Sobaniec S, Bernaczyk P, Pietruski J, et al. Clinical assessment of the efficacy of photodynamic therapy in the treatment of oral lichen planus. Lasers Med Sci 2013;28:311-6.
48. Mattsson U, Jontell M, Holmstrup P. Oral lichen planus and malignant transformation: is a recall of patients justified? Crit Rev Oral Biol Med 2002; 13:390-6.
49. Gándara-Rey JM, Freitas MD, Vila PG, et al. Malignant transformation of oral lichen planus in lingual location: report of a case. Oral Oncol EXTRA 2004;40:1-4.

Oral Lichen Planus – Known and Unknown

Maria Z. Mutafchieva1, Milena N. Draganova-Filipova2,3, Plamen I. Zagorchev4, Georgi T. Tomov1
1 Кафедра пародонтологии и заболеваний слизистой оболочки полости рта, Факультет дентальной медицины, Медицинский университет - Пловдив, Пловдив, Болгария
2 Кафедра медицинской биологии, Факультет медицины, Медицинский университет - Пловдив, Пловдив, Болгария
3 Технологический центр экстренной медицины, Пловдив, Болгария
4 Кафедра медицинской физики и биофизики, Факультет фармации, Медицинский университет - Пловдив, Пловдив, Болгария

Лишайниковый план – хроническое кожно-слизистое воспалительное заболевание, поражающее 1 - 2% населения, а максимальное распространение заболевания установлено среди женщин старше 40 лет. Его этиология остаётся неопределённой, и патогенез всё ещё является предметом серьёзного обсуждения. Оно считается аутоиммунным заболеванием, опосредованным главным образом Т-лимфоцитами. В настоящей работе представлены наиболее распространённые внешние агенты (в частности, вирусы), внутренние агенты, такие как белки стресса и теплового шока, которые рассматриваются в качестве «факторов запуска» и описывается активность различных клеток и белков, связанных с развитием этого заболевания. Диагноз основан на клинических и гистопатологических данных; также могут быть полезны прямые или косвенные методы иммунофлюоресценции. Несмотря на широкий спектр терапевтических моделей, эффективность лечения является недостаточной. В настоящее время местные кортикостероиды широко признаны в качестве стандарта для лечения, но также могут использоваться ретиноиды, ингибиторы кальциневрина и другие иммуносупрессанты. Ввиду характеристик этих препаратов приоритет отдаётся альтернативным безопасным методам, какими являются низкоинтенсивная лазерная терапия (НИЛТ) и лазерная терапия обеззараживания десневых карманов (ЛОТК). В наличной литературе существует противоречивые мнения относительно возможного предракового характера ОЛП, однако рекомендуется периодическое профилактическое обследование.