The Management of Oral Lichen Planus

A Peer-Reviewed Publication
Written by Jeff Burgess, DDS, MSD

Abstract
Oral Lichen Planus (LP), a disease defined as reticular, erosive, atrophic, or bullous in nature, is an immune mediated condition that typically develops in women in their fifth and sixth decade. Reticular LP, absent erythema, is asymptomatic and does not usually need intervention. However reticular LP associated with erythema or erosions needs treatment and periodic re-evaluation as there is potential for conversion to carcinoma. The literature suggests that erosive and ulcerated LP is best managed with topical corticosteroid preparations and in refractory cases, systemic steroids. Several other immunosuppressive medications and non-medication based interventions are also available but at greater cost and with greater potential for adverse reactions and side effects. This educational review article focuses on the best practices management of oral lichen planus.

Educational Objectives
At the conclusion of this educational activity participants will be able to:
1. Describe interventions used to manage oral lichen planus.
2. Identify the appropriate medications to be prescribed for managing erosive and ulcerative oral lesions.
3. Implement treatment strategies for managing oral ulcers associated with the disease.
4. Identify the interventions mentioned in the literature that are supported by limited evidence.

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Author Disclosure
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Oral Lichen Planus (LP), a disease defined as reticular, erosive, atrophic, or bullous in nature, is an immune mediated condition that typically develops in women in their fifth and sixth decade. Reticular LP, absent erythema, is asymptomatic and does not usually need intervention. However reticular LP associated with erythema or erosions needs treatment and periodic re-evaluation as there is potential for conversion to carcinoma. The literature suggests that erosive and ulcerated LP is best managed with topical corticosteroid preparations and in refractory cases, systemic steroids. Several other immunosuppressive medications and non-medication based interventions are also available but at greater cost and with greater potential for adverse reactions and side effects. This educational review article focuses on the best practices management of oral lichen planus.

Introduction
Lichen Planus (LP) is an immune mediated condition that can cause inflammation and erosion of the oral mucosa. Oral LP is characterized as reticular, erosive, atrophic, and bullous with the sub-diagnosis primarily based on clinical presentation. The condition typically develops in the fifth and sixth decade with women more likely to express the disease. It is rare in children. Disease prevalence rates for all forms of oral LP range from one percent to 6.3 percent. The prevalence rate for LP that causes mucosal erosion or erosive/bullous lesions is considerably less that the rate for reticular LP (one estimate: one percent of LP lesions) but a higher frequency of lesions may be reported because the symptoms associated with these latter problems tend to be more severe. The disease is often chronic with episodes of remission and reoccurrence.

Reticular LP without adjacent erythema is asymptomatic. Erosive/ulcerative LP (ELP) is associated with significant inflammation and tissue erosion, and sometimes bullous oral lesions. When this is the case the patient is likely to describe a continuous moderate to severe aching pain that at times feels like burning. Pain is worsened with eating (particularly spicy or hot foods) or when the lesions contact alcohol. Widespread distribution of lesions throughout the mouth can be quite debilitating.

The cause (or causes) of oral LP remains unclear but considerable research suggests that the primary disease mechanism is immune mediated. It is now thought that in most cases mucosal pathology is triggered by keratinocytes or modified Langerhans cells in either antigen specific (keratinocyte killing by CD8 cytotoxic cells) or antigen non-specific reactivity (mast cell degranulation and matrix metalloproteinase activation). It has also been proposed that in some cases of LP refractory to immunologic intervention the underlying cause may be partly neurogenic.

Other factors or conditions that are reported in relation to the development of mucosal lichen planus include genetics, infection (e.g. the Hepatitis C virus – even though the magnitude of the association may be minimal), medication effects (termed a lichenoid drug reaction), vitamin or mineral deficiencies (e.g. b-12 insufficiency and iron deficient anemia), systemic disease (e.g. autoimmune diseases such as Sjögren’s disease, rheumatoid disease, pemphigus or graft versus host disease, and amalgam hypersensitivity. The fact that oral LP results from an immune system abnormality, regardless of the above considerations, informs most treatment considerations related to patient care. If underlying disease or a lichenoid drug reaction is strongly suspected as the cause of oral LP the patient should be referred for additional medical evaluation or in the case of medication, medical consultation. Even though oral lichen planus has been associated with a number of medical problems, the treating clinician should not conclude that the patient with oral lichen planus also has one of these conditions. It has been proposed that as a general rule patients with LP should not be routinely screened for systemic disease.

Management
Reticular LP
Oral ‘reticular’ LP is typically asymptomatic and intervention is not usually necessary. However, because white plaques associated with whitened striations characteristic of the condition may be confused with oral cancer, the lesions of oral reticular lichen planus should be charted for location, photographed, and watched for changes indicative of potential dysplastic conversion (e.g. characterized by changes in size, thickness, and coloration of the mucosa, ulceration or erosion, and emergent symptoms such as pain). Dysplastic transformation of lichen planus is relatively rare. This is highlighted by a recent systematic review of over 7000 LP subjects where malignant transformation is reported to have occurred in 3.7 percent of cases. Similar ‘conversion’ statistics have been cited elsewhere. Transformation to malignancy is reported to occur more frequently in female patients with the most common site of expression the tongue. In one study cancer was found to develop a mean of 51.4 months from the time of the initial discovery of the condition. The Patients’ average age at onset of malignancy was 60.8 years. The take away from this is that if ‘transformation’ to a premalignant lesion (dysplasia) is suspected, histopathologic evaluation is indicated.
In patients with lichenoid lesions caused by hypersensitivity to amalgam or other restorative materials or who have lesions suggesting a ‘lichenoid drug reaction’ treatment consists of the removal of the associated restoration(s) or discontinuation of the offending medication (always under the guidance of the patient’s prescribing physician). Some of the types of medications associated with lichenoid drug reaction are the antihypertensives including beta-blockers, angiotensin converting enzyme (ACE) inhibitors, and diuretics, antibiotics (e.g. penicillamine, aminosalicylate sodium, isoniazid, rifampin, streptomycin, tetracyclines), non steroidal anti-inflammatories (NSAIDs), oral hypoglycaemic agents (for type 2 diabetes), the antiretroviral medications (to treat HIV), antimalarials (hydroxychloroquine), anticonfusants (e.g. carbamazepine, oxcarbazepine, phenytoin, valproate, antidiarrheals (e.g. bismuth), antifungals (e.g. amphotericin B, ketoconazole), and antihistamines (e.g. cimetidine, cinnarizine, tripolidine). A more extensive list can be found at: http://emedicine.medscape.com/article/1080772-overview.

Lichenoid reactions tend to be widespread over the mucosa while lesions associated with dental restorative material will be confined to the mucosa that is in close contact with the material. At present there appears to be little reason to remove all amalgam restorations in patients with generalized reticular lichen planus.19

**Erosive/ulcerative LP**

Erosive and ulcerative lichen planus is a chronic disease with no known cure. Regardless of therapy, complete resolution of lesions is difficult to achieve. Future research may ultimately tease out specific cellular and genetic mechanisms that prove useful in the development of effective long term treatment strategies and a possible cure. Until then the clinician treating oral erosive/ulcerative LP must make do by using pharmacotherapy that is known to suppress immune function, suppress pain, and promote healing or utilize other non-pharmacological interventions that have shown promise in managing the disease. Most medication strategies used to treat erosive/ulcerative LP have limited supportive evidence; and only a few are supported by studies using rigorous scientific methodology.20 There is even less evidence based support for non-pharmacological interventions such as photochemotherapy, photodynamic therapy, or laser therapy which have also been suggested as treatment for ERP.

**Pharmacotherapy**

In a Cochrane Database Systematic Review published in 2012 several authors reviewed studies found in multiple databases up to September 2009 including the Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, and LILACS and the registries for ongoing trials.21 They selected any RCT (randomized controlled trial) that reported results of treatment of lichen planus with topical or systemic medication. Unfortunately, they were only able to identify 15 randomized controlled trials (RCTs) with 473 total participants having erosive lichen planus; and they were not able to pool data due to the small number of subjects, the heterogeneity of the interventions, design methods, and the different outcome variables found between the studies. Meta-analysis could not be performed. Nonetheless, the authors report that in one study of 50 subjects, 0.025% clobetasol propionate administered as a liquid microsphere significantly reduced pain when compared to the delivery of a placebo ointment. In another study significant pain reduction occurred with a cyclosporine solution, with this contrasted to a 0.1% triamcinolone acetonide in orabase formulation. And in another study aloe vera gel was “six times more likely to result in at least a 50%” improvement in pain compared to placebo. Finally, it is noted that pimecrolimus cream was more effective in improving erosive lichen planus (ELP) than a vehicle cream.

Another Cochrane Database Systematic Review (published in 2011) assessed 28 clinical ELP trials that used pain report as an outcome variable following medication application and similar results are reported.22 In both of these studies the authors conclude that “there is only weak evidence for the effectiveness of any of the treatments for oral ELP”.

Nonetheless, topical corticosteroids continue to be widely considered in Medicine and Dentistry as first-line therapy for erosive and ulcerative LP.23 Additionally, high potency topical steroids are thought to be the most effective strategy for reducing symptoms and minimizing disease in patients with severe pathology. For example, in a double-blind, placebo-controlled clinical study a 75 percent improvement was reported following the application of fluocinonide in an adhesive base.24

High-potency topicals include clobetasol (Temovate), fluocinonide (Lidex), and halobetasol (Ultravate). All three are dispensed as 0.05% creams or ointments. Clobetasol propionate and fluocinonide are also provided in a 0.05% solution but the FDA has recommended that these products only be used externally because of the possibility of hypothalamus-pituitary-adrenal inhibition.25

Gels can be mixed with equal parts orabase to make an adhesive paste for application to small or medium sized lesions. It is recommended that lesions should be coated with the gel or cream after each meal and at bedtime.27 Broader coverage can sometimes be achieved through the use of an acrylic appliance that holds the gel or cream against the mucosa.

Dexamethasone, another potent corticosteroid, is effective in treating generalized erosive or ulcerative lesions. It is prescribed as a rinse that is held in the mouth for short time. When used three or four times daily maximum coverage is provided. Two prescriptions are presented: Rx: Dexamethasone (Decadron) elixir 0.5 mg/5ml (Disp 320 mls; Sig [1] For 3 days, rinse with 1 tablespoonful (15 mls) qid and swallow. Then [2], for 3 days, rinse with 1 teaspoonful (5ml) qid and swallow. Then [3], for 3 days, rinse with 1 teaspoonful (5ml) qid and swallow...
every other time. Then [4], rinse with 1 teaspoonful (5ml) qid and expectorate. Aother prescription is: Rx: Dexamethasone elixir 0.5mg/5 ml (Disp 100 mls; Sig: Rinse with 1 teaspoonful for 3-4 minutes qid and spit out); discontinue when lesions become asymptomatic. Research comparing these two prescriptions of dexamethasone has not been published so either approach should be considered reasonable intervention.28

Even with topical application of corticosteroid to mucosa, there is potential for systemic as well as local side effects. Close collaboration with the patient’s physician is recommended, particularly when these medications are prescribed for a prolonged period of time28 (this reference covers both the 1997 and 2001 versions of the Clinician’s Guide to Treatment of Common Oral Conditions). Systemic prednisone can also be prescribed but its use should be considered only in cases involving severe recalcitrant lesions where topical approaches to therapy have failed. If systemic corticosteroid is considered, it should be prescribed at the lowest possible dosage and only for a short time. There are a number of prescribing regimens that are effective. One is: Rx Prednisone tablets 5mg; Disp: 40 tabs; Sig: Take 5 tablets in the morning for five days, then 5 tablets in the morning every other day until gone. Medrol dose packs are also available.

Any patient using corticosteroid should be monitored for the emergence of fungal infection (candidiasis) which can occur with application of this class of drugs. If the LP patient is prone to fungal infections or experienced candida infection in the past following steroid administration, prophylactic antifungal therapy should be pursued as concurrent therapy.

Additional immunosuppressant medications and immunomodulatory agents that may be considered to manage severe recalcitrant erosive ulcerative LP include calcineurin inhibitors such as cyclosporine, tacrolimus, and pimecrolimus. However, there are few studies supporting the use of cyclosporine. Also, these drugs are expensive. Further, local and systemic side effects can be problematic.29

Pimecrolimus and tacrolimus, indicated for the treatment of atopic dermatitis, have a number of studies supporting their use in treating oral lichen planus. These drugs inhibit T-cell activation and cytokine release from mast cells. Systematic review of five double-blind studies, 10 prospective studies, as well as numerous case reports suggests that topical tacrolimus ointment 1% may be equal to topical clobetasol propionate 0.05% ointment and topical triamcinolone acetonide 0.1% paste in terms of treatment outcome.30 Treatment with topical tacrolimus appears to result in measurable blood levels but according to one author this medication has not been associated with significant adverse events.31 However, prolonged use of tacrolimus may increase cancer risk so if used, it should only be applied for a short period of time. The US Food and Drug Administration recommends against oral application of this medication to mucosa. http://www.fda.gov/safety/medwatch/safetyinformation/ucm283160.htm

Other medications such as the retinoids, dapsone, azathioprine, mycophenolate mofetil, acitretin, and enoxaparin that have been suggested for use with ELP have limited scientific support and should not be routinely utilized. The use of some of the above drugs, particularly long term, may result in adverse reactions. For example, two common side effects of dapsone use are hemolysis and hypersensitivity reactions in the form of fever and jaundice; and these effects typically occur within the first 6 weeks of therapy.25 Finally, all of the above drugs are also more expensive relative to the cost of corticosteroids.

Non-pharmacological Treatment Modalities

There are several non-pharmacological interventions suggested for treatment of ERP. These include PUVA therapy (this therapy uses an application of a sensitizing drug – psoralen – followed by ultraviolet light), Photodynamic therapy (the three components include a photosensitizer, light source, and tissue oxygen), and Laser therapy. Only the latter is likely to be utilized in the dental office. These strategies have limited supportive evidence for treating LP but might be considered for severe recalcitrant cases.32 When 21 atrophic erosive OLP patients treated with laser phototherapy (LPT) three times/week were compared to 21 atrophic erosive OLP patients using clobetasol propionate 0.05% applied three times a day and with both strategies utilized for up to three months the LPT group was found to have a higher percentage of complete lesion resolution at days 60 and 90 and with no recurrence of lesions. In contrast, the clobetasol group is reported to have experienced worsening of all the variables analyzed. Although this suggests that LPT may be quite effective in the treatment of recalcitrant ELP, an in-office application three times a week might be difficult for some patients to manage.34 PUVA therapy has been associated with adverse events including nausea and dizziness and 24 hour photosensitivity.35

Although not considered ‘treatment’, patients with oral lichen planus should be advised to maintain good oral hygiene and instruction in appropriate care should be considered to reduce injury to involved tissues. Dietary instructions should include instructions to eat soft nutritious foods during outbreaks, the avoidance of caffeine, and cessation of smoking and alcohol. Since ELP may be aggravated by stress and can be associated with depression, activities that reduce stress and modify depression should be suggested. Another novel approach to treatment that has not been extensively studied via RCTs but may be useful is antioxidant application (e.g. AO ProVantage Gel). In one case study (see images below) the gel was applied three times daily for eight weeks with symptom improvement continuing for over a year. Also, there is published evidence that the saliva in a patient with OLP exhibits increased levels of oxidative stress and lower antioxidant capacity compared to the saliva of healthy patients.37, 38, 39
Conclusion

Dentists are very likely to encounter one or more patients with oral lichen planus in the course of their careers. The odds are that they will encounter reticulated LP and differentiating this disease from other more serious problems such as dysplasia is important. But it is the erosive/ulcerative condition that will require direct intervention and careful monitoring. This course has described several pharmacologic approaches to treatment that are evidence-based or in common usage in managing erosive/ulcerative LP and has described non-pharmacologic interventions that may have limited use. Although a number of new drugs have been suggested as treatment of ELP, at the present time topical application of corticosteroid medication followed by systemic administration in severe refractory cases remains the standard of care.

Bibliography


Author profile

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Author Disclosure

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1. Which of the following statements most accurately characterizes lichen planus:  
   a. The condition develops in the third and forth decade  
   b. Men are most likely to express the disease  
   c. It is most prevalent in children  
   d. It is an immune mediated condition  

2. Which of the following statements is accurate:  
   a. Reticular lichen planus occurs more frequently than other forms of the disease  
   b. The prevalence rate for all forms of oral LP range from 1 to 6.3 percent  
   c. Both a and b  
   d. Neither a or b  

3. Oral lichen planus is characterized as:  
   a. Reticular  
   b. Erosive  
   c. Atrophic  
   d. All of the above  

4. Which of the following statements is not accurate:  
   a. Lichen planus is curable  
   b. Lichen planus is chronic with episodes of remission and reoccurrence  
   c. Erosive LP is associated with significant inflammation  
   d. Patients with erosive LP often say their mucosal is painful  

5. Which of the following statements is most true:  
   a. Generalized lichen planus associated with erosions is not usually debilitating  
   b. Erosive lichen planus is associated with moderate to severe aching pain  
   c. Pain with erosive lichen planus is not worsened by eating  
   d. Medications containing alcohol are not likely to aggravate LP erosive lesions  

6. The mucosal pathology of LP is thought to include:  
   a. Antigen specific activity involving keratinocyte killing by CD8 cytotoxic cells  
   b. Antigen non-specific reactivity involving mast cell degranulation and matrix metalloproteinase activation  
   c. Both a and b  
   d. Neither a or b  

7. Which of the following statements is most accurate:  
   a. A neurogenic etiology has been proposed to explain LP refractory to immunologic intervention  
   b. Langerhans cells have little to do with disease  
   c. Both a and b  
   d. None of the above  

8. Which of the following factors has been linked with lichen planus:  
   a. Vitamin A deficiency  
   b. Hepatitis C virus  
   c. Both a and b  
   d. Neither a or b  

9. When medications cause lichen planus the condition is termed:  
   a. Medication lichen planus  
   b. Medicamentosa  
   c. Erosive LP disease  
   d. Lichenoid drug reaction  

10. Medical conditions that have been associated with oral lichen planus include:  
    a. Pemphigus  
    b. Graft versus host disease  
    c. Rheumatoid disease  
    d. All of the above  

11. If a drug reaction is strongly suspected as the cause of oral LP the patient should be:  

Questions

12. Which of the following statements is accurate:  
   a. If a patient has lichen planus he/she is likely to have one of the medical conditions associated with the disease.  
   b. As a general rule patients with LP should not be routinely screened for systemic disease.  
   c. Both a and b  
   d. Neither a or b  

13. If a patient is found to have oral reticular LP a dentist should:  
   a. Aggressively treat the condition  
   b. Chart the condition for location and follow immediately biopsy  
   c. Assume that every lesion is precancerous  

14. Dysplastic transformation of lichen planus, while rare, may occur in what percent of cases per reported research:  
   a. 3.7  
   b. 5.1  
   c. 12.2  
   d. 1.0  

15. Which of the following statements accurately describes dysplastic conversion:  
   a. It occurs more frequently in female patients  
   b. The most common site of conversion is the tongue  
   c. The average age at conversion is around 60  
   d. All of the above  

16. Which of the following statements is most accurate:  
   a. Non-medication interventions used to treat erosive/ulcerative LP have been extensively researched  
   b. Few studies involving medication treatment are supported by rigorous science  
   c. Both a and b  
   d. Neither a or b  

17. Which class of medication is the most useful for treating erosive/ulcerative LP:  
   a. The antifungals  
   b. The anticoagulants  
   c. The corticosteroids  
   d. None of the above  

18. The clinician treating erosive/ulcerative LP should consider which of the following as first line therapy:  
   a. High potency corticosteroids  
   b. Low potency corticosteroids  
   c. An immunosuppressive such as Cyclosporine  
   d. None of the above  

19. A dentist treating erosive/ulcerative LP should not use which type of corticosteroid preparation:  
   a. Clobetasol (Temovate®) ointment  
   b. Fluocinonide (Lidex®) ointment  
   c. Halobetasol (Ultravate®) cream  
   d. Fluocinolone (Lidex®) solution  

20. What is the percentage of corticosteroid in high-potency topicals used to treat LP:  
   a. 0.20%  
   b. 0.05%  
   c. 0.10%  
   d. 0.75%  

21. When corticosteroid gels are used it is recommended that they be:  
   a. Applied four times a day  
   b. Applied before each meal  
   c. Applied twice a day after meals  
   d. None of the above  

22. The correct way to prescribe dexamethasone is:  
   a. 0.5 mg/5mls, Disp 320 mls; Sig – for 3 days rinse with 1 tablespoonful (or 15mls) qid and swallow; then for 3 days rinse with 1 teaspoonful (or 5mls) qid and swallow; then for 3 days rinse with 1 tsp qid and swallow; then rinse with 1 tsp qid with expectoration  
   b. 0.5mg/5ml, Disp 100 mls; Sig – Rinse with 1 teaspoonful (5mls) for 3-4 minutes qid and spit out; Discontinue when lesions are asymptomatic  
   c. Both a and b  
   d. Neither a or b  

23. When should systemic prednisone be prescribed:  
   a. Immediately after lesions are diagnosed  
   b. Only in cases involving severe recalcitrant lesions where topical therapy has failed  
   c. When the patient has both reticular as well as erosive/ulcerative lesions  
   d. None of the above  

24. What is the most accurate approach to prescribing systemic prednisone:  
   a. It should be prescribed at the lowest possible dosage  
   b. It should be prescribed for a long period of time  
   c. It should be prescribed using an increasing dose strategy  
   d. None of the above  

25. Adverse reactions to prescribed systemic prednisone include:  
   a. Hypothyroidism-pituitary-adrenal inhibition  
   b. Fungal infection (candidiasis)  
   c. Both a and b  
   d. Neither a or b  

26. Additional immunosuppressant medications and immunomodulatory agents that can be considered to manage recalcitrant erosive/ulcerative LP include:  
   a. Cyclosporine  
   b. Tacrolimus  
   c. Pimecrolimus  
   d. All of the above  

27. Which statement is accurate regarding Tacrolimus use for erosive/ulcerative LP:  
   a. The US Food and Drug Administration recommends against oral application of this medication  
   b. Tacrolimus may increase cancer risk  
   c. Tacrolimus treatment can result in measurable blood levels  
   d. All of the above  

28. Which statement accurately reflects medications such as the retinoids, dapsone, azathioprine, mycophenolate, mofetil, and acitretin:  
   a. There is limited scientific support for their use  
   b. These drugs have few side effects or adverse reactions  
   c. Dapsone has not been associated with hemolysis and hypersensitivity reactions  
   d. All of the above  

29. Of the following non-pharmacological interventions suggested as treatment of erosive/ulcerative LP, which therapy has been contrasted with Clobetasol:  
   a. PUVA therapy  
   b. Photodynamic therapy  
   c. Laser phototherpay  
   d. None of the above  

30. PUVA therapy has been associated with which of the following:  
   a. Nausea  
   b. Dizziness  
   c. Photosensitivity  
   d. All of the above
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