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Overview of Diagnosis and Treatment Options of Lichen Planus

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Abstract: **We aimed by this review, to discuss the recent concepts in the diagnosis and treatment modalities of Lichen planus (LP), also overviewing the clinical features of this dermatological disease which will support the diagnostic procedures. Computerized search was performed using following databases; CENTRAL, PUBMED, MEDLINE, and EMBASE. for all published studies concerning Lichen Planus up to March, 2017., using the term ''lichen planus'', and searched PubMed, using the Medical Subject Heading (MeSH) term ''lichen planus'' and free-text words such "diagnosis", "pathogenesis", Clinical features" and " treatment". we restricted our search to only English published articles with human subjects. Topical corticosteroids are regularly utilized for LP. Betamethasone valerate, fluocinonide, and clobetasol-17-propionate are the only corticosteroids with adequate evidence to recommend a greater helpful effect than placebo in the treatment of LP. Short-term use of oral corticosteroids for flare-ups in OLP might be advantageous.**

Keywords: **Lichen planus (LP), Medical Subject Heading (MeSH), Clinical features.**

1. INTRODUCTION

Lichen planus (LP) is a chronic mucocutaneous condition of the stratified squamous epithelium that influences genital and oral mucous membranes, skin, nails, and also scalp [(1)]. Oral lichen planus (OLP) is the mucosal counterpart of cutaneous LP [(2)]. It is derived from the Greek word "leichen" indicates tree moss and also Latin word "planus" implies level [(3)].

The disease influences 1 - 2% of the populace, it is seen clinically as reticular, papular, plaque-like, abrasive, atrophic or bullous types. Intraorally, the buccal mucosa, tongue and the gingiva are typically included although various other sites may be rarely impacted [(4,5,6)]. Oral mucosal lesions existing alone or with concomitant skin sores. The skin lesions existing as violaceous flat-topped papules in ankles, wrist, and genitalia, yet characteristically the face skin is saved [(5,6)].

The etiology as well as pathogenesis of OLP has actually been the focus of much research, and several antigen-specific and also nonspecific inflammatory devices have been put forward to describe the pathogenesis. Although mostly palliative, a range of therapy methods is in method, from topical application of steroids to laser treatment [(6,7)]. Therapeutic administration could frequently be challenging as well as might call for a multidisciplinary strategy to consist of gynecologists, dentists, and skin doctors. The emphasis of therapy is to reduce the patient's pain and pain throughout daily activities such as eating, drinking, speaking, or intercourse, as well as enhancing quality-of-life procedures. Other than clinical treatment, preserving careful oral hygiene, regulating oral plaque with routine in-office cleansings, and getting rid of the infection are all critical for handling OLP [(8,9)].

Timeless cases of lichen planus may be detected scientifically, but a 4-mm strike biopsy is usually valuable and is required for even more irregular cases. High-potency topical corticosteroids are first-line therapy for all kinds of lichen planus, consisting of cutaneous, genital, and also mucosal abrasive lesions [(10)]. In addition to clobetasol, topical tacrolimus appears to be a reliable treatment for vulvovaginal lichen planus. Topical corticosteroids are also first-line therapy for mucosal erosive lichen planus. Systemic corticosteroids ought to be considered for serious, prevalent lichen planus involving oral, cutaneous, or genital sites. Oral immunosuppressant needs to be thought about for patients with serious lichen planus that does not react to topical therapy [(10)].

We aimed by this review, to discuss the recent concepts in the diagnosis and treatment modalities of Lichen planus (LP), also overviewing the clinical features of this dermatological disease which will support the diagnostic procedures.

2. METHODOLOGY

Computerized search was performed using following databases; CENTRAL, PUBMED, MEDLINE, and EMBASE. for all published studies concerning Lichen Planus up to March, 2017., using the term ''lichen planus'', and searched PubMed, using the Medical Subject Heading (MeSH) term ''lichen planus'' and free-text words such "diagnosis" , "pathogenesis", Clinical features" and " treatment". we restricted our search to only English published articles with human subjects.

3. RESULTS

- **Pathophysiology of LP:**

Although the exact etiology of lichen planus is unknown, an immune-mediated pathogenesis is acknowledged [(6)]. A meta-analysis of primarily case-control research studies conducted in numerous countries discovered a statistically significant association between hepatitis C virus (HCV) infection and lichen planus, [(11)] although there is no recognized explanation for this association. Compared to the control group, patients with lichen planus had a higher prevalence of HCV direct exposure (chances ratio = 5.4; 95% confidence period, 3.5 to 8.3), and patients with HCV infection had actually an increased occurrence of lichen planus (odds ratio = 2.5; 95% self-confidence period, 2.0 to 3.1) [(11)]. It is appropriate to screen all patients with lichen planus for HCV infection [(12)].

- **Clinical Features of Lichen planus:**

Lichen planus lesions are explained utilizing the 6 features (**Table 1**). Onset is normally acute, affecting the flexor surface areas of the wrists (**Figure 1**) [(13)], forearms, and legs. These sores are frequently covered by lacy, reticular, white lines referred to as Wickham striae (**Figure 2**) [(13)]. The lesions might appear in a direct configuration, following the lines of trauma [(12)]. Initially, LP appears as a mucosal and cutaneous eruption, though rarely it can manifest with only oral or nail findings. LP typically begins as discrete, flat-topped papules that are 3 to 15 mm in size which may coalesce into larger plaques. Early in course of the disease they appear red, but quickly they take on reddish purple or violaceous hue. The center of the papule may be somewhat umblicated and its surface area is covered by particular, extremely fine grayish white lines, called Wickham striae. The lesions can occur anywhere on the skin surface however often are located on the flexor surfaces of limbs, inner elements of knees and thighs and trunk and also might appear on lines of trauma, reflecting the Köbner phenomenon [(14)]. The face frequently stays uninvolved. The primary symptom of LP is extreme pruritis. The intensity of pruritus differs [(15)]. Some patients report genital participation with features much like skin sores [(16)]. scalp participation (lichen planopilaris), and nail beds. Rarely, there is laryngeal, esophageal and conjunctival involvement [(15,16)].

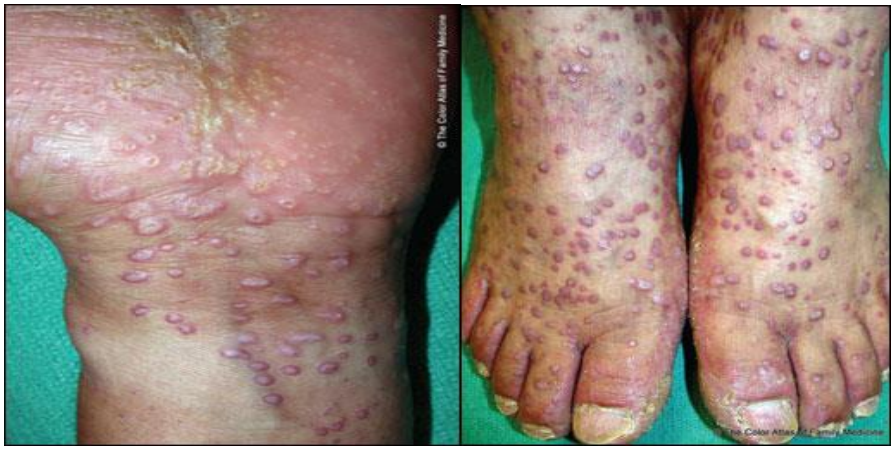

Figure 1: Lichen planus with papules and plaques on the wrist Figure 2: Lichen planus on the feet.

Cutaneous lichen planus might present in various types. Direct lichen planus manifests as closely aggregated linear sores on the limbs that may establish the Koebner phenomenon. Annular lichen planus (**Figure 3**) accounts for roughly 10

percent of lichen planus cases [17]. It commonly looks like arcuate groupings of individual papules that develop rings or a peripheral extension of clustered papules with main clearing. In addition to the usual sites of distribution, this kind of lichen planus might take place on male genitalia and buccal mucosa [17]. Atrophic lichen planus (Figure 4) is an unusual form that is characterized by a few well-demarcated white, pink, or bluish papules, spots, or plaques with superficial atrophy. Hypertrophic lichen planus, normally occurs on the extremities, particularly the ankles, shins, and interphalangeal joints, and it tends to be the most pruritic kind [17]. It is often chronic with recurring scarring and pigmentation when lesions clear. In vesiculobullous lichen planus, vesicles or bullae develop from preexisting lesions on the lower limbs, back, or butts, or in the mouth. Erosive/ulcerative lichen planus sores develop within oral sores or begin as waxy semitranslucent plaques on the soles [18].

Table1: The Six P's to Describe Lichen Planus Lesions

Planar (flat-topped)
Purple
Polygonal
Pruritic
Papules
Plaques

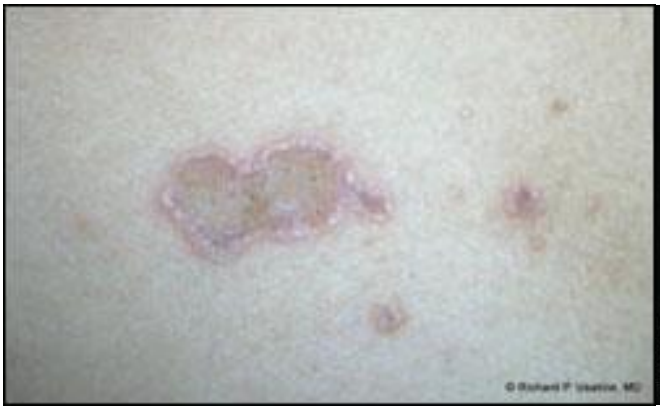

Figure 3: Annular lichen planus on the breast

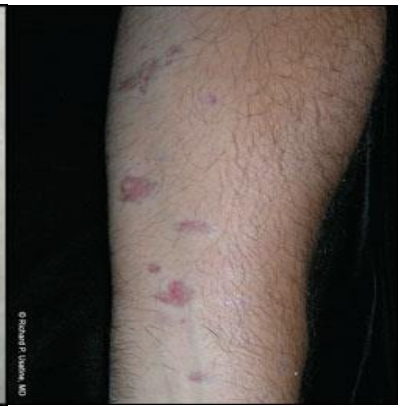

Figure 4: Atrophic lichen planus

- **Oral Lichen Planus Manifestations:**

In the mouth, the disease presumes somewhat various scientific look than on the skin, and is characterized by lesions consisting of radiating white, gray, creamy, thread-like papules in a direct, annular and retiform arrangement forming typical lacy, reticular spots, streakes and rings. A small white elevated dot exists at the crossway of white lines known here as striae of Wickham as compared to Wickham striae in skin [15]. The lesions are asymptomatic, bilaterally/symmetrically anywhere in the oral cavity, [19] but most typical on buccal mucosa, tongue, lips, gingiva, floor of mouth, taste buds and might appear weeks or months before the look of cutaneous lesions (**Figure 5 & 6**).

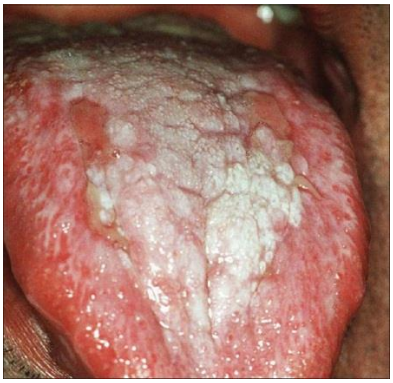

Figure 5: Plaque type lichen planus–lesion on tongue

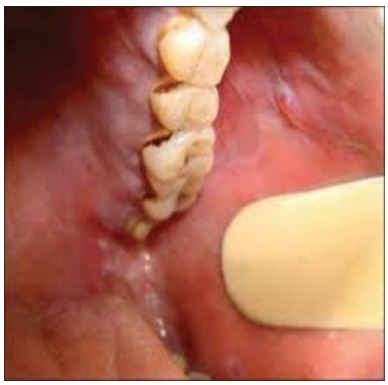

Figure 6: Bullous type LP on upper buccal mucosa

- **Diagnosis procedures of LP:**

Lichen planus can be detected scientifically in traditional cases, although biopsy is frequently valuable to validate the diagnosis and is needed for more irregular presentations. A 4-mm punch biopsy should be adequate on the skin or in the mouth. The histology shows a particular "saw-tooth" pattern of epidermal hyperplasia; hyperparakeratosis with thickening of the granular cell layer; and vacuolar alteration of the basal layer of the epidermis, with an intense infiltration (primarily T cells) at the dermal-epidermal junction. A 4-mm punch biopsy of perilesional skin for direct immunofluorescence might be added to the workup when bullous lesions, pemphigus, or bullous pemphigoid is present. (**Tables 2 and 3**) present the differential medical diagnosis of oral and cutaneous lichen planus [20,21].

Table 2: Differential Diagnosis of Cutaneous Lichen Planus

CONDITION	*DISTINGUISHING FEATURES*	*TREATMENT*
Eczema	Excoriations and lichenification of skin, often on flexor surfaces	Topical steroids and emollients
Lichen simplex chronicus	One or more plaques with lichenification in an area that is easily scratched	Potent topical steroids; help patient avoid scratching and picking at skin
Pityriasis rosea	Herald patch preceding annular plaques with collarette scale	Reassurance (self-limited condition)
Prurigo nodularis	Pruritic nodules, often on the extremities	Potent topical steroids, oral antipruritic medications, help patient avoid scratching and picking at skin
Psoriasis	Plaques with thick scale on extensor surfaces	Potent topical steroids, topical vitamin D, other treatments

Table 3: Differential Diagnosis of OLP

CONDITION	*DISTINGUISHING FEATURES*	*DIAGNOSTIC METHOD*	*TREATMENT*
Bite trauma	White area on buccal mucosa where the teeth occlude	Clinical appearance	Reassurance
Leukoplakia	White adherent patch or plaque on oral mucosa that does not rub off	Punch or shave biopsy	Surgical excision or cryotherapy with liquid nitrogen
Thrush	White adherent patch or plaque on oral mucosa that rubs off	Clinical appearance and potassium hydroxide (KOH) preparation	Antifungal suspension or troches

- **Treatment strategies for LP and especially OLP:**

Corticosteroids have actually been the mainstay of management of LP; yet, other techniques like calcineurin inhibitors, retinoids, dapsone, hydroxychloroquine, mycophenolate mofetil and enoxaparin have actually contributed substantially toward treatment of the disease. Analysis of current data on pathogenesis of the disease suggests that obstructing IL-12, IFN-γ, MMP-9, rantes, or tnf-α activity or upregulating TGF-β1 activity in LP might be of restorative value in the future [22].

Corticosteroids treatment:

These are the most frequently used group of drugs for the treatment of LP [23]. The rationale behind their use is their capability to regulate inflammation and immune reaction. They act by lowering the lymphocytic exudate and supporting the lysosomal membrane [24]. Topical midpotency corticosteroids such as triamcinolone acetonide, high-potent fluorinated corticosteroids such as fluocinonide acetonide, disodium betamethasone phosphate, and more just recently, superpotent halogenated corticosteroids such as clobetasol are utilized based upon the intensity of the sore. The best disadvantage in using topical corticosteroids is their absence of adherence to the mucosa for an enough length of time. Although trials were done utilizing topical steroids in addition to adhesive base, no research study shows their superiority when compared to steroids without the base (carboxymethyl cellulose) [25]. The exact same research study likewise recommends the usage

of adhesive paste utilized for dentures, which contains just non-active active ingredients as a lorry to bring the topical application. This has shown outstanding bioadhesive homes, due to its high molecular weight (above 100,000) and the versatility of the polymeric chain. Accessible and small erosive lesions found on the gingiva and taste buds can be dealt with by the use of an adherent paste in a made-to-measure tray (custom-made tray), which allows for precise control over the contact time and makes sure that the whole lesional surface area is exposed to the drugs [26]. Patients with extensive kinds of OLP are recommended superpotent and high-potent corticosteroids mouthwashes and intralesional injections. Long-lasting use of topical steroid can result in the advancement of secondary candidiasis which requires antifungal treatment [24]. The prospective tachyphylaxis and adrenal deficiency is high when using superpotent steroids like clobetaso l, especially when utilized for a longer amount of time. Systemic corticosteroids are booked for recalcitrant erosive or erythematous LP where topical methods have stopped working. Systemic prednisolone is the drug of option, but should be used at the lowest possible dose for the quickest duration [23].

Calcineurin & Cyclosporine:

Calcineurin is a protein phosphatase which is involved in the activation of transcription of IL-2, which promotes the growth and differentiation of T-cell response [26]. In immunosuppressive therapy, calcineurin is hindered by tacrolimus, cyclosporine and pimecrolimus. These drugs are called calcineurin inhibitors.

Cyclosporine, a calcineurin inhibitor, is an immunosuppressant utilized extensively in post-allogenic organ transplant to minimize the activity of patient's immune system. This selectively reduces T-cell activity, the primary reason for transplant rejection, and hence boosts the uptake of the foreign organ. Cyclosporine binds to the cytosolic protein cyclophilin of immunocompetent lymphocytes, specifically T-lymphocytes. This complex of cylosporine and cyclophilin prevents calcineurin, which under regular circumstances induces the transcription of IL-2. They likewise prevent 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. Nevertheless, the service is prohibitively pricey and should be reserved for highly recalcitrant cases of OLP. Systemic absorption is very low [23].

Tacrolimus & Pimecrolimus:

Tacrolimus, also a calcineurin inhibitor, is a steroid-free topical immunosuppressive agent approved for the treatment of atopic dermatitis. It is 10 - 100 times as powerful as cyclosporine and has higher percutaneous absorption than cyclosporine. It has been successfully utilized in recalcitrant OLP cases. This substance is produced by Streptomyces tsukubaensis and comes from the macrolide family. The immunosuppressive action of tacrolimus is similar to that of cyclosporine, although it has a greater capability to penetrate the mucosa. It prevents the first stage of T-cell activation, inhibiting the phosphatase activity of calcineurin. Burning sensation is the commonest adverse effects observed; relapses of OLP after cessation have likewise been observed. The United States Food and Drug Administration has recently issued a potential cancer risk from the prolonged use of tacrolimus and has recommended its use for brief periods of time and not continually [22,23,25].

Pimecrolimus prevents T-cell activation by preventing the synthesis and release of cytokines from T cells. Pimecrolimus likewise prevents the release of inflammatory cytokines and arbitrators from mast cells. 1% topical cream of pimecrolimus has actually been effectively used as treatment for OLP. Pimecrolimus has considerable anti-inflammatory activity and immunomodulatory capabilities with low systemic immunosuppressive potential [21].

Retinoids & Efalizumab:

Topical retinoids such as isotretinoin, fenretinide and tretinoin, with their immunomodulating homes, have been reported to be efficient in OLP. Reversal of white striae can be accomplished with topical retinoids, although results may only be momentary. Systemic retinoids have been used in cases of severe lichen planus with variable degree of success. The positive impacts of retinoids should be weighed against their rather significant adverse effects like cheilitis, elevation of serum liver enzymes and triglyceride levels and teratogenicity [27,28].

It is a recombinant humanized monoclonal antibody which is used as an immunosuppressant in the treatment of psoriasis. Efalizumab, a monoclonal antibody to CD11a, binds to this adhesion particle and triggers improvement in OLP by decreased activation and trafficking of T lymphocytes. In vitro research studies of mononuclear cells in OLP have shown a decrease of 60% in migration by peripheral blood mononuclear cells after pretreatment with anti-CD11a antibodies. It is administered when a week as a subcutaneous injection. It is presently an approved drug for the treatment of plaque psoriasis [29].

PUVA therapy & Photodynamic treatment:

This non-pharmacologic method utilizes photochemotherapy with 8-methoxypsoralen and long wave ultraviolet light (PUVA). Psoralens are substances discovered in numerous plants, making the skin momentarily 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 utilized in the treatment of serious cases of OLP [30]. When this medicine is taken orally, 2 major downsides of PUVA treatment include the negative results of nausea and lightheadedness secondary to psoralen and 24-hour photosensitivity. Dosimetry can be hard within the complicated geometry of the mouth, because PUVA is normally administered on skin over large, open surface areas [31].

Photodynamic treatment (PDT) is a method that uses a photosensitizing substance like methylene blue, triggered at a particular wavelength of laser light, to damage the targeted cell through strong oxidizers, which trigger cellular damage, membrane lysis, and protein inactivation. PDT has actually been used with relative success in the field of oncology, notably in head and neck tumors. PDT is discovered 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 [32].

4. CONCLUSION

Topical corticosteroids are regularly utilized for LP. Betamethasone valerate, fluocinonide, and clobetasol-17-propionate are the only corticosteroids with adequate evidence to recommend a greater helpful effect than placebo in the treatment of LP. Short-term use of oral corticosteroids for flare-ups in OLP might be advantageous. OLP patients might partially gain from topical retinoids as a second-line therapy. Tacrolimus can be used as a secondline therapy when topical corticosteroids are inadequate. In addition, pimecrolimus may be considered as a corticosteroid-sparing representative although there is only strong evidence of enhancing the indications but not the symptoms.

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