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THE VERSATILITY OF EXCIMER LASER IN ORAL LICHEN PLANUS

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ABSTRACT:
Oral lichen planus (OLP) is a chronic,immune mediated inflammatory condition primarily composed of T cells which commonly affects the muco-cutaneous parts of the body. Current treatment strategies aim to manage the disease morbidity through lifestyle modifications and pharmacological interventions. However, OLP often shows frequent relapses and also develop potential adverse effects due to the long term use of steroids which are the first-line medication for OLP.Consequently, alternative management approaches are required to address the heterogeneous nature of this condition. The 308-nm excimer laser has demonstrated efficacy in the treatment of various inflammatory and pigmented lesions in dermatology. This specific 308-nm monochromatic laser has been shown to be highly effective which directly target the inflammatory components of OLP lesion thereby providing symptomatic relief in patients. This study aims to review the application of excimer laser for the management of oral lichen planus.

INTRODUCTION:

Laser therapy in oral and maxillofacial medicine has gained excellent popularity for its painless, bloodless and scarless approach. Today lasers are widely employed in various Oro-mucosal lesions. Laser dates back to 1959 when Albert Einstein first explained this property of lasers to amplify the light intensity in order to produce highly focused beams of a specific wavelength which are considered to be uni-directional and coherent(1).Einstein 's theory proposed stimulated and spontaneous emission which explains three key elements of lasers: monochromaticity, where all the waves have equal energy and frequency; coherence, meaning the waves are synchronized in their specific speed; and collimation, ensuring that the waves maintain the parallelism without divergence(2).

These are generated as a result of the “excited dimers” formed from a mixture of a noble gas(xenon) and a halide (halogen chloride gas) dissociates and repels among each other hence the term “Excimer”(3).These dissociated dimers produces a 308-nm ultraviolet (UV)which predominantly penetrates the epidermal cells and subsequently the fibroblasts(4).

Oral lichen planus is a T-cell mediated chronic inflammatory response affecting the mucosa of the oral cavity with global prevalence of about 2%.(5) OLP exists in different forms such as reticular, atrophic, erosive, plaque, bullous and papillar. Among which the erosive type of OLP as higher potential for malignant transformation. The antigen presentation by basal keratinocytes leads to the activation of CD4+ helper T cells thereby stimulating the release of pro-inflammatory mediators such as Tumor necrosis factor-alpha (TNF-α) and interferon-gamma (6). These inflammatory T cells are directly targeted by 308 nm excimer lasers in OLP.

The use of laser technology in the treatment of epidermal lesions is well-established, but its application in managing mucosal lesions is gaining significant popularity due to its painless and scarless properties(7).

Erosive lichen planus, considered the most resistant type to conventional treatment modalities, has been successfully treated with laser therapy. In that context, this paper aims to review the application of excimer laser for the treatment of OLP and also the outcomes of such procedures.

HISTORICAL ASPECTS OF LASERS:

1903	*Finsen*	Carbon arc lamp with lenses and filters for the management of lupus vulgaris
1960	*Fritz Houtermans*	Excimer laser
1963	*Leon Goldman*	Effects of lasers in dental caries and other hard tissues of oral cavity
1970-1975	*Nikolai Basov et al*	Xenon dimer (Xe2), halides (originally Xe Br)
1983	*Rangaswamy Srinivasan* and *Stephen Trokel,* ophthalmologist	Excimer laser in medical applications(8)
1997	*Bonis and colleagues*	308-nm excimer laser in the field of dermatology for the treatment of refractory psoriasis(9)

MECHANISM OF ACTION OF EXCIMER LASER ON TISSUE:

The 308-nm excimer laser is composed of a mixture of inert gases xenon, argon, krypton and combined with a reactive gas like fluorine or chlorine that forms unstable "excited dimers"(10). The dissociation of these dimers generates a 308-nm ultraviolet monochromatic coherent wavelength within the spectrum which are readily absorbed by biological tissues. These rays disrupts the molecular bonds of the targeted lesion, causing a controlled ablative cure(11)(Fig-1).

This wavelength primarily passes throughout the entire length of tissue penetrating the epidermal cells and then the fibroblasts. This ultraviolet B light prompt apoptosis, rendering it a suitable option for inflammatory lesions. Key immunological chromophores, such as nuclear DNA, absorb UVB radiation, resulting in DNA damage that reduces T-lymphocyte proliferation.

Furthermore, UVB radiation increases upregulation of the tumor suppressor gene p53 leading to cell cycle arrest in keratinocytes and T lymphocyte subsequent apoptosis. It also exhibits immunomodulatory properties, which involves the suppression of antigen-presenting cells, modulation of the Th1 phenotype towards a Th2 response and induction of regulatory T-lymphocytes (12).

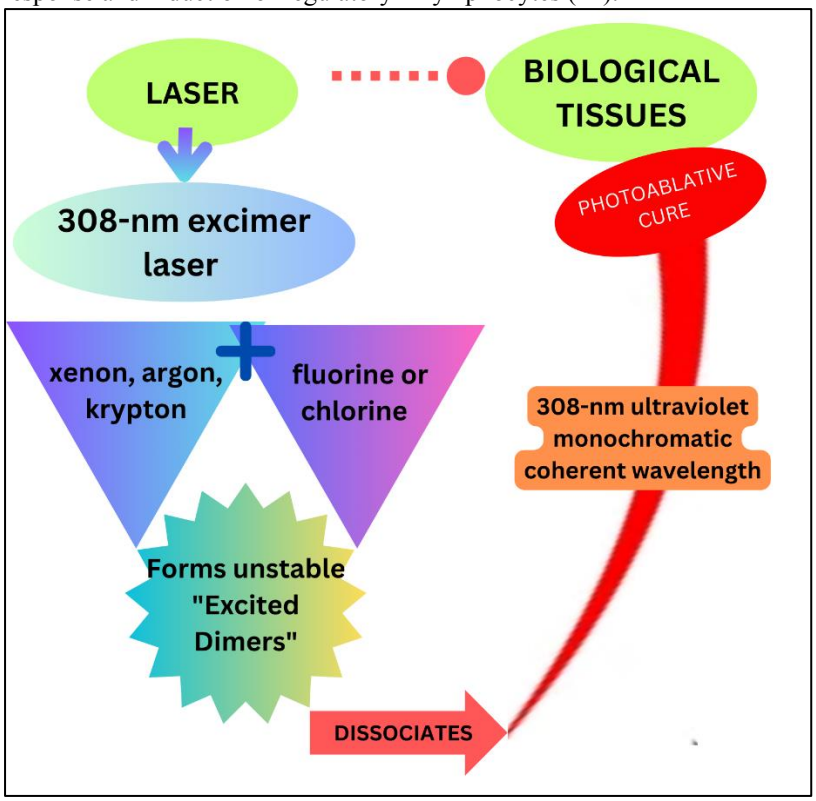

Fig-1-Mechanism of action of excimer laser

APPLICATION OF EXCIMER LASERS IN DERMATOLOGY:

It is a form of phototherapy that is Ultraviolet (UV) radiation or visible light employed in the field of dermatology for the treatment of various conditions. When compared to narrow-band UV phototherapy, the 308-nm excimer laser appears to enhance and accelerate the re-pigmentation process in vitiligo(13) When used in combination with other topical treatments, the 308-nm excimer laser demonstrated greater effectiveness for the management of psoriasis, than when used as monotherapy(14).It has been approved by the FDA for the treatment of psoriasis, leukoderma, vitiligo and other hypopigmented lesions(15) The 308-nm excimer laser has demonstrated its efficacy in treating a range of inflammatory and pigmentary skin conditions, including vitiligo, psoriasis, atopic dermatitis, alopecia, lichen planus, cutaneous T-cell lymphoma, Langerhans cell histiocytosis, localized scleroderma, and genital lichen sclerosis(16).

And also Excimer lasers (193 nm), due to their unique physical properties, can be used to perform photoablation on the cornea of eye and selectively remove corneal tissue in order to correct refractive errors in the corneal refractive surgery which explains its potential for safety profile.(17)

CONVENTIONAL TREATMENT APPROACH FOR OLP:

Oral lichen planus (LP) is an autoimmune, idiopathic, chronic T cell mediated inflammatory condition that affects the skin, mucous membranes, nails, and hair(18) OLP occurs in approximately 60% to 70% of patients with cutaneous LP, 20% develop genital lesions(19).OLP lesions appears as whitish radiating striae ,lacy (Wickham's Striae)or erythematous patches or plaque like lesion to painful ulcerations. Based on the clinical presentation six clinical subtypes of OLP are as follows reticular, papular, plaque, atrophic, erosive, and bullous(20). Around two-thirds of individuals with oral lichen planus experience symptoms, which exhibits cycles of exacerbation and quiescence. Buccal mucosa is the most commonly affected site followed by gingiva, tongue, labial mucosa and lip with typically bilateral distribution (21).

The antigen-specific mechanism proposes that antigen presentation by Langerhans cells or basal keratinocytes triggers the activation of CD4+ helper T cells, which then stimulate the release of pro-inflammatory T-helper 1 cytokines like TNF -alpha and interferon-gamma (22). This in turn induces a cytotoxic reaction mediated by CD8+ T cells, targeting the epidermal basal cell layer and resulting in keratinocyte apoptosis.

In OLP various other specific and non-specific disease mechanism,(i) Endothelial cells of the subepithelial vascular network show heightened expression of the vascular adhesion molecules CD62E, CD54, and CD106. The infiltrating lymphocytes express complementary receptors to these vascular adhesion molecules(23),(ii)Nonspecific mechanisms such as mast cell degranulation and MMP-1 activation further stimulates the accumulation of T-cells, disrupt the basement membrane(BM) through mast cell proteases, and induce keratinocyte apoptosis(24).Additionally, the release of cytokines and chemokines directly recruits more immune cells,perpetuating the inflammatory response with TNF-α, IFN-γ, and IL-1,(iii)MMP-9, which cleaves collagen-IV are upregulated in OLP lesional T cells, resulting in enhanced BM disruption(25).(iv) The recruited mast cells undergo degranulation in response to RANTES, which leads to the release of chymase and TNF-α. These substances then stimulate increased RANTES production by the lesional T cells of OLP.(v)

Treatment for oral lichen planus is typically aimed at symptomatic management and often fails to achieve satisfactory outcome. Topical steroids are often the first line of therapy. Yet their long term use has a well-known spectrum of adverse effects like candidiasis. Clinicians may consider other adjunctive therapy topical anesthetics, cyclosporine, tetracycline, retinoids, tacrolimus and systemic corticosteroids,cyclosporine,retinoids,dapsone,phenytoin,Azathioprine,Levamisole,cyclophosphamide,Thalidomide,hydroxychloroquine,griseofulvin,Extracorporeal photochemotherapy and Psoralen-UV-A(26).

CLINICAL AND PATIENT OUTCOME OF EXCIMER LASER IN TREATMENT OF OLP:

Numerous treatment modalities have been explored in many clinical trials in order to manage OLP and aims to alleviate corticosteroids' side effects, which are considered the gold standard therapy for OLP. Perhaps treatment of such symptomatic recurrent lesions represents a mystifying therapeutic challenges for the clinicians. Current strategies aims to treat the disease according to its pathogenesis .Low-dose treatment with the excimer 308-nm laser is one among them which demonstrated overall improvement in symptomatic OLP and erosive variant.

Kollner K et al in 2003 conducted a study for eight patients with OLP who were treated using the 75 to 150 mJ/cm² powers of 308-nm UVB excimer laser three times a week, up to 32 sessions.Out of eight patients clinical improvement was observed in six patients. Two patients attained complete remission, but one of them experienced a recurrence of the lesions after 4 weeks. The study found that pain was effectively managed during the 10 sessions, and there were no signs of lesion progression observed in the three-month follow-up period.(27). *Manju Trehan et al* in 2004 treated clinically and histopathologically proven nine symptomatic OLP patients who were unresponsive to conventional therapies with low-dose 308-nm excimer laser radiation at an initial dose of 100 mJ/cm^2 once a week, upto 7 months. Five patients exhibited remarkable clinical and

subjective improvement following seven treatment sessions. In every session, VAS was recorded and perfect photograph was taken (28). *Wei-Bing Liu et al* in 2017 provided treatment for six OLP patients with 308-nm excimer laser, of which clinical symptoms significantly improved in five patients of which three patients showed partial remission in the size of the lesion(29*). Germi et al* in 2008 conducted a study on 22 histologically proven OLP patients where individual lesions were processed with 308 nm excimer laser device. The regression of the disease was associated with the clinical presentation and size of the lesion. In general, the reticular, atrophic forms and plaque form healed more quickly than compared to the erosive forms and symptoms related to it decrease proportionately(30).

TREATMENT PROTOCOL AND PARAMETERS FOR 308 nm EXCIMER LASER:

(i)This device produces UV-B with a monochromatic wavelength at 308 nm.(ii)The laser has a chamber containing xenon and chloride gas as its lasing medium, generating a stream of 30-nanosecond pulses at a rapid repetition rate of up to 250 Hz.(iii)For mucosal lesions, the excimer laser features an angled optical handpiece with a power output 142 mW/cm² which can deliver laser light to the oral mucosa with a spot size of 6 × 6 mm. (iv)The working handpiece: Narrow flexible fiber-optic handpiece, circular in shape with a diameter of 8 mm, which produces a power density of 48mW/cm².(v)The distal end of the handpiece has an exchangeable tip (vi)After each use, the tip is removed and cleaned with disinfectant agents. (vii)Both the patient and the laser operator must wear UV-protective safety goggles. (viii)For narrow-band UVB phototherapy at 311 nm, the starting dose is typically low, with incremental increases of 50 millijoules/Sq cm. A maximum dose of 400 mJ/cm^2 was administered at any given session. (ix)Patients receive a single phototherapy session per week, lasting 5 seconds, with 7 to 30 sessions needed to achieve the desired outcome. Yet some studies have reported that bi-weekly management with excimer has showed potentially enhanced remission response leading to overall reduction in cumulative dose. (x)Participants are carefully reevaluated to assess any potential effects from the previous session. Probable side effects (31) associated with Excimer laser are hyperpigmentation, blisters, erosions, burning pain, and koebnerization.

COMMENTS:

The primary aim of OLP management includes moderation of symptoms with lifestyle changes, pharmacologic and non-pharmacological measures thereby minimizing the morbidity associated with the lesion. One such adjuvant alternative modality is laser therapy which are well adapted in the field of dermatology and dentistry, provides minimally invasive procedures with less discomfort to the patient and achieved remarkable esthetic outcomes in various oro-mucosal lesions (32). Excimer laser is one type of phototherapy that emits a 308-nm wavelength of monochromatic UV- B light in high-intensity at brief pulses. Its potential benefit is its accuracy and precision, as it directly targets the affected area sparing the surrounding healthy tissue. It is commonly employed in such types of recalcitrant conditions like lichen planus where most of the conventional treatments does not show a significant resolution outcome. The fundamental action of excimer laser is to cause T-cell depletion by affecting key mediators of apoptosis basal cell membrane and decreasing the rate of proliferation of keratinocytes of oral mucosa On other hand it also leads to an elevation in the levels of the pro-apoptotic regulator p53 which in turn exhibit its implicit anti-inflammatory property (33)

CONCLUSION

After intriguing assessments from various clinical trials of application of Excimer laser 308 nm it appears to be an efficient and well-tolerated therapy, showing satisfactory response in subjects with oral lichen planus. Its effectiveness is associated to immunosuppression property towards oral mucosa showing drastic reduction in inflammatory reaction of this lesion.

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