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Photodynamic Therapy: An Effective Non-Invasive Treatment for Oral Lichen Planus

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Abstract: Oral lichen planus (OLP) is a chronic inflammatory mucosal condition with a multifactorial etiology, often presenting as atrophic or reticular lesions that cause significant discomfort and impair quality of life. Traditional treatment modalities, including corticosteroids, provide symptomatic relief but are associated with potential side effects and recurrence. This study evaluates photodynamic therapy (PDT) as a non-invasive, effective, and patient-friendly treatment for OLP.We employed 0.2% methylene blue as a photosensitizer for 10 minutes and applied PDT for 2 minutes per site, delivering 12 joules of energy per session in contact mode.Atotal of six sessions were conducted on patients diagnosed with atrophic and symptomatic reticular OLPvariants. Clinical outcomes were assessed using the VisualAnalog Scale (VAS) for pain and discomfort. Remarkable improvement was observed, with the mean VAS score reducing from 9 to 0 post-treatment. The treatment demonstrated excellent tolerability, absence of adverse effects and significant symptom relief.PDT offers a promising alternative to conventional therapies, addressing the need for a minimally invasive and recurrence-freeapproach. Its efficacy, safety, and patient acceptability underscore its potential to redefine OLP management strategies. Further randomized controlled trials with larger sample sizes are warranted to establish PDT as a standard care modality for OLP.

Keywords: Photodynamic therapy (PDT), Oral lichen planus(OLP), Non-invasivetreatment, Methylene blue, Minimally invasive therapy, Visual Analog Scale (VAS)

Introduction

Oral lichen planus (OLP) is an autoimmune, common, chronic T-cell-mediated inflammatory disorder of the skin and mucous membranes that occurs in various clinical forms that often pose a diagnostic and therapeutic challenge due to its refractory course and relapsing nature. First described in 1869 by British physician Wilson Erasmus, lichen planus (LP) is an autoimmune condition affecting the skin, hair, eyes, mucous membranes and nails. When the lesions are present in the oral cavity, it is referred to as oral lichen planus (OLP), with OLP being found in 53.6% of cutaneous LP patients.

The term "Lichen" originates from the Greek word "Leichen," which refers to moss on trees. In some sources, lichens are described as primitive plants formed by a symbiotic relationship between algae and fungi. "Planus" is a Latin word meaning flat, suggesting the interpretation of a flat fungal condition. Ferdinand Ritter von Hebra (1816–1880), a dermatologist, first described a skin disease known as "Oral Ruber Planus" in1860 and referred to it as Lichen Ruber. The term "Lichen Planus" was later introduced by British dermatologist Erasmus Wilson in 1869. In 1893, Thibierge described oral lichens as appearing symmetrically, and in 1895, Wickham detailed the characteristic striae.Andreasen later identified six clinical forms of the condition, and Dubreulith provided the microscopic description of Oral Lichen Planus (OLP). In 1910, Francois Henri Hallopeau reported the first Case of carcinoma related to OLP.

Oral Lichen Planus (OLP) is an immune-mediated condition characterized by diverse clinical manifestations and an unpredictable course marked by periods of remission and exacerbation.

It is classified into six clinical forms: reticular, papular, plaque-like, atrophic, erosive, and bullous. The reticular form is characterized by a lacy network of white lines known as Wickham striae and is typically asymptomatic. The papular form presents as raised white papules that may resemble other lesions, while the plaque-like form appears as white patches or plaques on the oral mucosa. The atrophic form involves areas of erythema with a loss of normal mucosal architecture, often leading to discomfort. In contrast, the erosive form features painful ulcerations and erythematous areas, prompting patients to seek treatment due to significant discomfort. Lastly, the bullous form is characterized by fluid-filled vesicles that can rupture, resulting in erosive lesions. These forms may manifest individually or simultaneously, and the predominant clinical morphology can change over time, necessitating careful monitoring and management due to the potential for complications, including malignant transformation associated with the erosive and atrophic forms.

Various invasive and non-invasive treatments are recommended for managing Oral Lichen Planus (OLP), including local and systemic corticosteroids, laser therapy, and surgical procedures. While cutaneous lesions typically improve spontaneously following treatment, OLP often requires prolonged corticosteroid therapy and long-term follow-up.

However, extended use of corticosteroids in chronic OLP cases can lead to both local and systemic complications, such as opportunistic candidiasis, mucosal atrophy, adrenal insufficiency, gastrointestinal issues, hypertension, and diabetes. Although corticosteroids have been the gold standard in the treatment of OLP due to their anti-inflammatory and immunosuppressive properties, they are contraindicated in immunocompromised patients, including those with diabetes or hypertension, as these medications can further weaken the immune response. In such cases, photodynamic therapy (PDT) presents an ideal

alternative treatment option. PDT utilizes light-sensitive compounds along with specific wavelengths of light to effectively target and reduce lesions, offering a safer approach for patients who cannot tolerate corticosteroids. This method may provide symptomatic relief while minimizing the risk of adverse effects associated with systemic corticosteroid use. Given these considerations, this case series aims to evaluate the efficacy of PDT in the treatment of Oral Lichen Planus.

Patients in this case series commonly reported experiencing a burning sensation while consuming food, which significantly impacted their oral comfort and quality of life. Clinical examination of the oral cavity revealed characteristic lesions consistent with oral lichen planus (OLP), including erythematous patches, white striations, and erosive areas, thereby confirming the diagnosis. These findings underscored the symptomatic nature of OLP in the participants, warranting therapeutic intervention.

Participants were also required to demonstrate their willingness to adhere to the treatment protocol, which included consistent attendance for photodynamic therapy (PDT) sessions and follow-up visits. All participants provided written informed consent after receiving a detailed explanation of the procedures' potential risks and benefits.

For treatment, patients rinsed their mouths with 5 ml of 0.2% methylene blue, used as a photosensitizer, for 10 minutes to ensure adequate penetration into the lesions. After rinsing, the photosensitizer was retained on the lesions, and diode laser illumination was applied for 2 minutes per site, delivering 12 joules of energy per site. The treatment was administered twice a week for six weeks, with an interval of 3 to 4 days between sessions, resulting in a total of 12 sessions per patient.

Visual Analog Scale (VAS) scores were recorded at each visit to monitor changes in symptom severity, particularly pain and burning sensation. Post-treatment evaluation involved comparing pre-treatment and post-treatment VAS scores to assess the efficacy of PDT in reducing symptoms associated with OLP.

Case Report 1:

A 42-year-old female patient visited the department with a chief complaint of burning sensation in the oral cavity for the past six months. The patient reported no relevant medical or personal history.No cutaneous lesions were present. Intraoral examination revealed an ill-defined erythematous region with peripheral radiating white striae on the marginal and interdental papillae of teeth 11, 12, 13, 14, 15, 16, 17, 21, 41, 42, 43, 44, 45, 46, 47, and 48. The patient rated a pain intensity score of 8on the Visual Analog Scale (VAS). A Provisional diagnosis of erythematous oral lichen planus with desquamative gingivitis was given. Oral candidiasis was ruled out after an exfoliative cytology. She was advised oral prophylaxis and photodynamic therapy (PDT) for at least six weeks, with sessions scheduled twice a week. At the end of the treatment period, the patient reported a VAS score of 0, indicating significant relief from the underlying burning sensation.

PRE - OP	POST - OP
	

Case Report 2:

A 70-year-old female patient visited the department with a chief complaint of burning sensation in her mouth for the past two months. She had previously seen her local dentist for the same issue and was referred to our institute. The patient has been taking anti-anxiety medications for six years and antihypertensives for ten years. No cutaneous lesions were noted on extraoral examination. Intraoral examination revealed multiple well-defined white hyperkeratotic striae on the left buccal mucosa, extending from the distal aspect of tooth 37 to the mesial aspect of tooth 35. The patient rated her pain with a Visual Analog Scale (VAS) score of 9. Hospital Anxiety and Depression Scale(HADS) revealed abnormal scores for Anxiety and Depression. A Provisional diagnosis of Symptomatic Reticular oral lichen planus secondary to psychosomatic disorders was given.

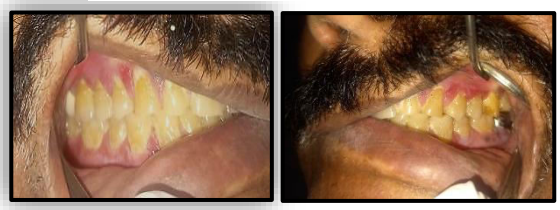
She was advised to undergo oral prophylaxis along with enameloplasty of the mesiobuccal cusp of tooth 36, followed by 12 sessions of photodynamic therapy (PDT) over six weeks. She showed improvement after six weeks, with complete elimination of symptoms occurring over a period of 1.5 years.

PRE - OP	POST - OP
	

Case Report 3:

A 70 year old male patient visited the Department with the chief complaint of burning sensation in his mouth since 3 months. Patient is diabetic and hypertensive since 10 years and is on medication. On extraoral examination, patient was well oriented to time, place and person and no cutaneous lesions were present. On intraoral examination, multiple ill defined regions of erythema were noted irt marginal and interdental gingiva of 12, 13, 23, 24, 25, 43, 44. Patient

gives a VAS score of 7 along with elevated scores for anxiety and depression for HADS score. Oral candidiasis was ruled out after an exfoliative cytology. A Provisional diagnosis of atrophic oral lichen planus was given. Patient was advised to undergo oral prophylaxis, followed by 12 sessions of photodynamic therapy (PDT) over six weeks. He showed improvement after six weeks, with complete elimination of symptoms occurring over a period of 6 months.

PRE - OP	POST - OP
	

Case Report 4:

A 25-year-old female patient with a history of juvenile diabetes presented with ulceration and a burning sensation in the inner aspect of her left cheek, which had persisted for two months and was exacerbated by spicy foods. She had previously visited a local dentist, who advised the extraction of her upper left wisdom tooth, which she underwent 1.5 months ago, resulting in the resolution of the ulceration but not the burning sensation. Upon examination, multiple lacy white keratotic striae were noted on the left and right buccal mucosa, suggestive of oral lichen planus (OLP). The patient reported significant pain, scoring 9 out of 10 on the Visual Analog Scale (VAS), and her assessment using the Hospital Anxiety and Depression Scale (HADS) indicated elevated levels of anxiety and depression. A Provisional diagnosis of symptomatic reticular oral lichen planus secondary to psychosomatic disorders was given.The patient was advised to undergo photodynamic therapy (PDT), which she completed over twelve sessions in six weeks, leading to an improvement in her VAS score from 9 to 5.

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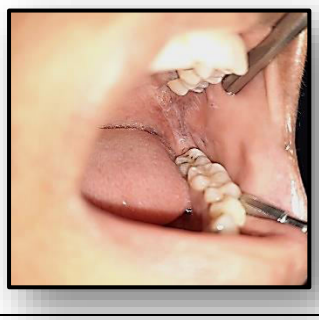	

Case Report 5:

A 33-year-old female patient presented to the department with a chief complaint of a burning sensation in the oral cavity for the past six months. She had previously visited three dentists who recommended corticosteroid-based ointments, but she experienced no relief from these treatments. The patient has a medical history of polycystic ovarian syndrome (PCOS) and was on hormone regulation pills. Upon extraoral examination, she was well-oriented to time, place, and person, with no abnormalities noted and no cutaneous lesions present. Patient had recent blood tests which revealed multiple nutritional deficiencies. Intraoral examination revealed multiple white hyperkeratotic striae on the left and right buccal mucosa. The patient rated her pain as 9 on the Visual Analog Scale (VAS). A provisional diagnosis of symptomatic reticular oral lichen planus was given. Following this assessment, she was advised to undergo 12 sessions of photodynamic therapy (PDT) over six weeks. Patient began to show improvement within two weeks and achieved complete elimination of symptoms by the end of the six-week treatment period.

PRE - OP	POST - OP
	

Discussion:

Photodynamic therapy (PDT) is an effective, easy-to-use, and safe treatment modality that combines the use of a photo sensitizer and light to induce cell and tissue damage. The photosensitizer is activated by exposure to low- level visible light at an appropriate wavelength. The concept of PDT was first described in 1900 by Raab and Tappeiner, who observed the cytotoxic effects of acridine on malaria-causing protozoa and identified the fluorescence properties of the compound. This led to the discovery of the "photodynamic phenomenon," where the interaction of light and a photosensitizer induces cellular damage. Later, Tappeiner and Jesion applied this phenomenon in the treatment of skin cancers.PDT involves the use of photosensitizers, which are chemical compounds that absorb light and, in the presence of oxygen, producer active species like singlet oxygen ($^1O_2$)and superoxide(O_2^-).These reactive pecies cause direct and

indirect cytotoxic effects, resulting in cell damage. The depth of light penetration in human tissue is determined by the photosensitizer's properties and the light wavelength. Red light, especially at wavelengths around 630 nm – 700nm, efficiently penetrates tissues and, when combined with a photosensitizer, allows for deeper tissue penetration, typically ranging from 0.5 cm at 630 nm to 1.5 cm at around 700 nm. This makes PDT suitable for a range of superficial and deep-seated lesions. Upon exposure to light of a specific wavelength, the photosensitizer transitions from its ground state to an excited state, which may further transition to a higher- energy triplet state. This high-energy state interacts with oxygen in the body, producing cytotoxic free radicals and singlet oxygen. The location of photosensitizer accumulation within the cell determines the type of cell death: accumulation in lysosomes or cell membranes leads to necrosis, while accumulation in mitochondria induces apoptosis. The inflammatory and immune response induced by PDT is another important aspect. Studies in mouse models have shown significant infiltration of neutrophils, mast cells, and monocytes, along with the activation of specific T-lymphocytes and apoptosis in hyperproliferating inflammatory cells. These immune responses contribute to the therapeutic effect of PDT by promoting the resolution of inflammation and targeting affected cells. Despite PDT's promising potential, there is significant variability in study outcomes due to differences in treatment protocols, which complicates comparisons across studies. These variations include the selection and application of photo sensitizers, light dosage, fluence rates, and light sources. Common photo sensitizers used for PDT in oral diseases include aminolevulinic acid (ALA), methylene blue, and to luidine blue. In some studies, 8 applications over 1 month have been used, with 50 µLof toluidine blue (1 mg/ml) combined with laser irradiation for 2.5 minutes at a fluence of 1.5 J/cm² and power density of 10 mW/cm² at 630 nm. In contrast, other studies used methylene blue solutions at varying concentrations and light sources (diode laser or LED), with irradiation parameters such as power densities ranging from 100 to 130mW/cm² and fluence values of 120 J/cm² over multiple sessions.

In our study, we employed a 0.2% methylene blue solution as the photosensitizer, combined with a diode laser emitting light at 660 nm. The treatment consisted of twelve applications over six weeks, with each session delivering affluence of 2.49J/cm² and apower density of 200mW/cm². This approach was selected to assess the effectiveness of a lower concentration of methylene blue, which has shown promising results in previous studies while minimizing the potential side effects of higher concentration.

Although PDT has demonstrated effectiveness in treating conditions such as actinic keratosis, basal cell carcinoma, and more recently, oral lichen planus (OLP),there is a lack of standardized treatment protocols. The lack of clear guidelines regarding the optimal photosensitizer concentration, light exposure time, and number of treatment sessions makes it difficult to draw definitive

conclusions about PDT's efficacy in OLP treatment.
Therefore, further studies with standardized protocols, larger sample sizes, and long-term follow-up are needed to validate PDT as a first-line treatment for OLPand to establish optimized treatment regimens for different presentations of the disease.

Conclusion:

In conclusion, photodynamic therapy (PDT) using 0.2% methylene blue demonstrated significant efficacy in alleviating the symptoms of atrophic and symptomatic reticular variants of oral lichen planus, as evidenced by marked reductions in VAS scores. The non-invasive nature and targeted approach of PDT make it a promising alternative to conventional therapies. However, further research with larger cohorts and extended follow-up is warranted to validate these findings and optimize treatment protocols. PDT has the potential to enhance the quality of life for patients with symptomatic OLP, offering a novel and effective therapeutic option in clinical practice.

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