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Low-level laser therapy as an adjuvant in the treatment of erythema multiforme of the oral mucosa: a case report

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ABSTRACT

Erythema multiforme is an autoimmune condition that can affect the skin and mucosa. Oral lesions initially present with edema and progress to superficial erosions with pseudomembrane formation. The most recommended treatment is the use of corticosteroids; however, low-level laser therapy can be effective in the treatment of erythema multiforme. We report a case of erythema multiforme in the oral mucosa treated with low-level laser therapy. A 73-year-old woman using alendronate for osteoporosis, losartan, and puran T4 with extensive ulcers on the upper and lower lips. The clinical diagnosis was erythema multiforme. The proposed treatment was 0.05% clobetasol propionate in gel, 3 times a day, and seven sessions of low-level laser therapy on alternate days. Low-level laser therapy significantly improved the erythema multiforme of the oral mucosa, offering the patient a non-invasive approach with no side effects.

Key words: erythema multiforme, treatment, low-level laser therapy, photobiomodulation, laser.

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Introduction

Erythema multiforme (EM) is an immune-mediated condition that can involve skin and mucous membranes.[1] Classically, the lesions present as ulcers and blisters that are characterized by target lesions symmetrically distributed on the extremities and trunk.[2,3] However, EM can be seen in dentistry, and the onset of the condition results in the need for immediate diagnosis and care.[3] EM has a wide spectrum of clinical and histological manifestations, which has led to controversy over the distinction between EM, Steven Johnson syndrome, and toxic epidermal necrolysis.[4-9] Thus, oral lesions resulting from systemic diseases represent a very large clinical challenge in terms of therapy, mainly due to the relationship with autoimmune diseases that require treatment based on corticotherapy, which can cause several side effects to the patient.

Low-level laser therapy (LLLT) was discovered in 1967 by Endre Mester at Semmelweis Medical University in Hungary.[7] Since those days, photobiomodulation (PBM) has made and continues to make, great strides in understanding the mechanisms of action at the molecular, cellular, and tissue levels.[10] Thus, many diseases, conditions, and therapeutic fields are becoming amenable to the beneficial effects of PBM.[7]

So, LLLT is a very valid option for the treatment of oral lesions associated with many of these pathologies, such as lichen planus, pemphigus vulgaris, erythema multiforme, and aphthous ulcers. Among the benefits of laser therapy, we can mention the ease of application by the professional, and the almost absence of side effects from the use of laser, we emphasize that an adequate treatment plan can be extremely effective for the treatment of the patient and improvement of signs and symptoms. In the present study, we aim to report a clinical case of erythema multiforme with extensive lesions on the lip, which was fully controlled with the use of low-level laser therapy associated with high-potency topical corticosteroids.[8,9]

Case Report

A 73-year-old female patient sought the stomatology service complaining of an ulcerated lesion with painful symptoms in the upper and lower lips. Evolution time of 1 year. During this time, the patient sought other dentists, but no proposed treatment was effective. Past dental history revealed that a previous incisional biopsy had been performed and the histopathological medical report was actinic cheilitis. Treatment with imiquimod, 250 mg, was unsuccessful. Past medical history revealed weekly use of alendronate for osteoporosis, losartan, and puran T4. Investigation for harmful habits was carried out, but nothing of note was observed. In the intraoral examination, he observed extensive ulcers on the upper and lower labial mucosa, which caused bleeding and a lot of pain (Figure 1). The clinical hypothesis was erythema multiforme. The proposed treatment was the use of 0.05% clobetasol propionate in gel, 3 times a day, and seven PBM sessions on alternate days. The device used for PBM was THEPAPY XT with wavelength in the red range (660nm), power of 40mw, energy density of 60J/cm2, and application time of 20 seconds per point. Infrared band of 880nm, power of 10mw, density of 60J/cm2, application time of 20 seconds per point. The patient improved significantly with the use of topical corticosteroids and LLLT applications (Figure 1).

Discussion

EM is an autoimmune disease that can affect the skin and mucosa.[1] Mucosal lesions can cause prodromic weakness, fever, and malaise.[11,12] Although the oral cavity is the most affected, oral lesions can be extremely painful.[1] As for the etiology, infections are associated in most cases, mainly those caused by herpes simplex virus (HSV) type 1 and HSV type 2. Drugs such as non-steroidal anti-inflammatory drugs, antiepileptic drugs, and antibiotics can cause EM. The antibiotics sulfonamide, penicillin, erythromycin, nitrofurantoin, and tetracycline are the most linked to the development of EM.[3] Other etiologic factors can cause EM; however, the incidence is low.[1,11,13] In the present case, the patient used some routine medications, but no medication is part of the risk group for the development of EM, and we had no information about other possible etiological causes.

Clinically, EM on the skin starts as pink or red papules, which can turn into plaques that can cause burning or itching. In the first five days, the EM can take on a different appearance. The inveterate lesion of erythema multiforme is called target or iris lesion. It is a round lesion of three concentric segments: a dark center, surrounded by a lighter pink ring, both surrounded by a

red ring.[1-3] While mucous membrane EM usually involves the labial mucosa, buccal mucosa, free gingiva, and lip vermilion. The initial clinical feature is erythema with edema and progresses to superficial erosions with pseudomembrane formation[11-13] which corroborates the history and the clinical findings of this case. However, mucosal EM involvement can vary in severity.

Treatment for oral mucosal MS may vary in the degree of involvement. Patients with minimal involvement can be treated with high-potency topical corticosteroids while patients with more debilitating involvement can be treated with systemic corticosteroids (*i.e.*, prednisone 40-60 mg/d with drug weaning over 2-4 weeks).[12,14] Although corticosteroids are the most frequent approach in the treatment of EM, our patient was first treated by another healthcare professional with an immune response modulator, imiquimod, without success. Thus, after our evaluation and diagnosis, topical corticosteroid and LLLT were performed.

Photobiomodulation therapy, in recent years, has played an influence on *in vitro* and *in vivo* studies related to oral medicine. Because PBM is based on the interaction of photochemical mechanism and intracellular mitochondrial chromophores that are light-absorbing molecules, laser energy is converted into metabolic energy by the respiratory chain with the production of adenosine triphosphate (ATP).[14,15] Thus, a cascade of reactions is activated allowing: i) acceleration of electron transfers in the respiratory chain attributed to changes in redox properties;[16] ii) conversion of energy into heat, defining the rise in temperature of the chromophore in a transient way;[16] iii) singlet oxygen;[16] iv)

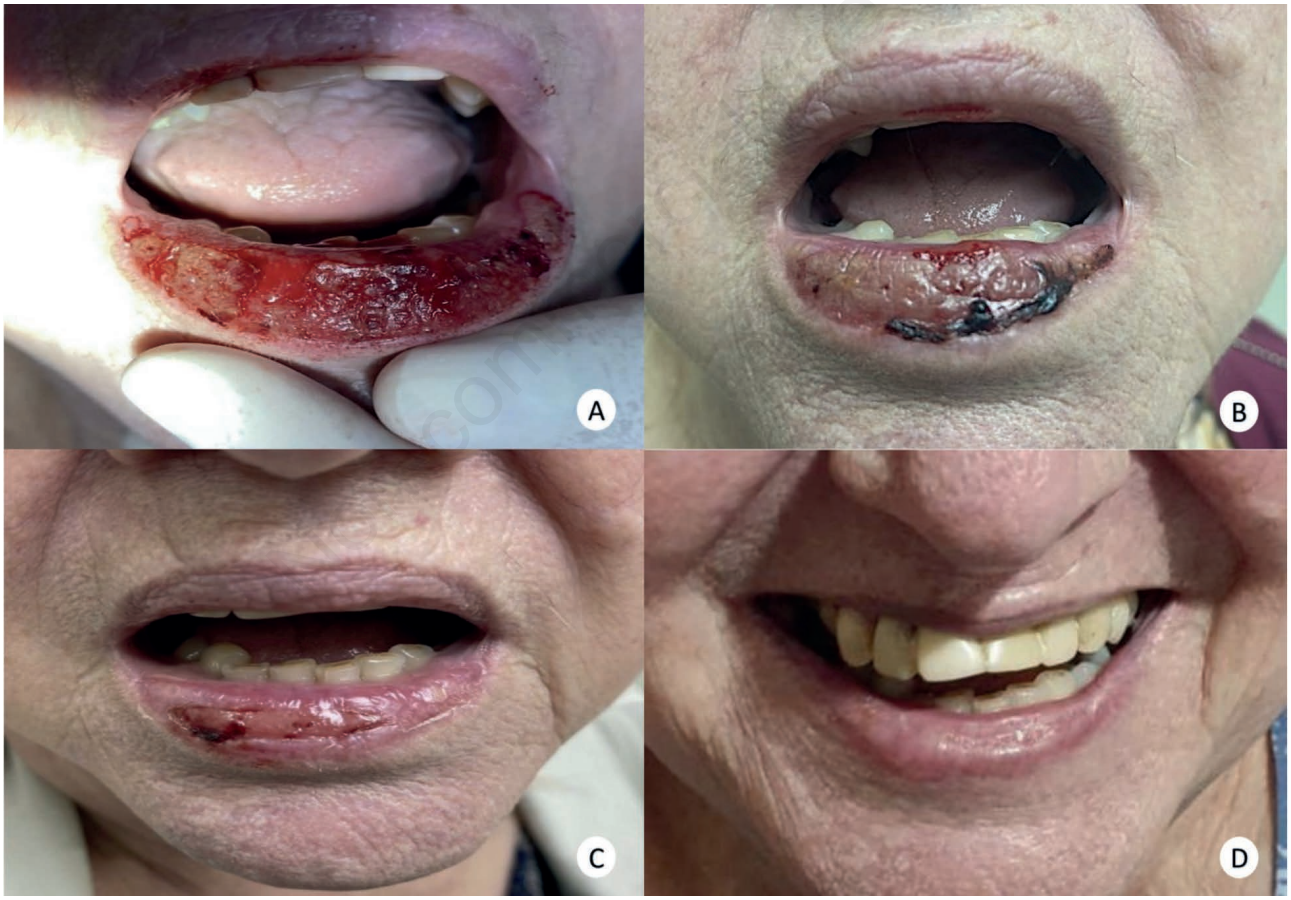

Figure 1. Initial clinical feature and follow-up. A) Initial clinical appearance, ulcerated lesion in vermilion of upper and lower lips; B) clinical feature after the third photobiomodulation session; C) clinical appearance after the 5th photobiomodulation session; D) clinical presentation after the 7th photobiomodulation session.

reabsorption of superoxide anions by mitochondria[16] and v) the NO hypothesis that laser irradiation could reverse the partial inhibition of the catalytic center by NO and ultimately increase the rate of binding and respiration by O_2.[17] While the secondary mechanisms of PBM include the activation of different intracellular signaling pathways, they regulate nucleic acid and protein synthesis, enzyme activation, cell cycle progression, and various transcription factors.[18] The activation of these primary and secondary factors is responsible for the so-called tertiary effect that is linked to cell proliferation and migration and protein synthesis is responsible for the systemic effect.[18] Still, it is known that the EM pathogenesis pathway suggests a trigger of autoreactive T cells by viral cells (HSV). Inflammatory responses are initiated by the recruitment of CD4+ T-helper 1 (Th1) cells.[19] Interferon-gamma (IFN-y) generated by this response upregulates cytokines and chemokines that amplify cutaneous inflammatory events, with an increase in circulating leukocytes, monocytes, natural killer (NK) cells, and autoreactive T cells to the epidermis.[19] Thus, PBM may be promising as an anti-inflammatory agent and reduce these and other components in autoimmune diseases, as seen in the present case. Furthermore, it offers a unique approach as it is non-invasive and without side effects, as autoimmune diseases are treated with corticosteroids that have a multitude of undesirable systemic consequences.[20] However, it is worth mentioning that the complete understanding of the pathogenesis of EM and the effects of PBM in autoimmune diseases is not clear, making it impossible to understand the mechanism of action of PBM in MS.

In summary, our case emphasizes the treatment of EM of the oral mucosa with LLLT and how much there was a significant clinical improvement with the use of PBM. However, it is important to emphasize that there is a lack of scientific evidence regarding the pathogenesis of EM and the effects of PBM in autoimmune diseases. The present case report presents a possibility for future investigations of LLLT as a treatment of autoimmune diseases with oral or systemic presentation.

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Ethical approval: all procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Consent for publication: consent for publication was obtained for every person's data included in the study.

Availability of data and materials: all data generated or analyzed during this study are included in this published article.

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