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ORAL LICHEN PLANUS: FROM DIAGNOSIS TO TREATMENT

Narrative Review

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ABSTRACT: Oral lichen planus is classified as chronic inflammatory mucocutaneous disease, its etiology is still unknown, however, it is known that its pathogenesis is well explained, studies show that cytotoxic lymphocytes-T induce apoptosis of the basal layer keratinocytes leading to the chronic inflammatory process, so it is called as an autoimmune disease. The present study aims to show the diagnosis and the most recent treatments available for Oral Lichen Planus in dentistry. To that end, a literature review was held based on books and scientific articles found in online platforms such as Scielo (Scientific Eletronic Library Online), PubMed, Lilacs (Latin American and Caribbean Literature in Health Sciences) and Google Scholar in Portuguese, English and Spanish. Some external and internal factors can be associated in its development as virus (Hepatitis C), medications, restorative materials (amalgam), genetic predisposition and psychological disorders (stress, anxiety and depression) that may cause physiological changes in the immune system, leading to the emergence or worsening of autoimmune diseases such as Oral lichen planus. In oral mucosa, Oral lichen planus can present itself in 6 clinical forms: reticular, erosive, atrophic, plaque, papular, and bullous. According the World Health Organization, Oral lichen planus has the potential to become malignant, but it is still a much debated issue in the literature, generating much controversy. It's treatment can be pharmacological and non-pharmacological. The pharmacological

treatment of first choice is corticoids, and the second choice is calcineurin inhibitors. The non-pharmacological treatment is being used more recently and involve the use of low-level laser and ozone therapy.

KEYWORDS: Corticosteroids. Lichen Planus. Oral Pathology.

INTRODUCTION

Oral Lichen Planus (OLP) is characterized as a mucocutaneous pathology, classified as chronic inflammatory, its etiology is still unknown, however, it is believed that its appearance is the result of an abnormal immune response mediated by T lymphocytes.[1,2] Although it may occur at any age, most of the first manifestations occur between the fourth and seventh decade of life, with an average age between 50 and 55 years, it is more frequent in women since on average 60% to 70% are female.[3]

Although the etiology is unknown, there are several factors that may influence its appearance, such as: diabetes, drugs, stress, anxiety, intestinal diseases, medications, hypertension, viral infections, autoimmune diseases, dental materials (amalgam), genetic predisposition and neoplasms. Although its etiology is not clear, its pathogenesis is well defined.[4,5] OLP can manifest in different ways: reticular, erosive, atrophic, plaque, papular and bullous. The different forms may occur simultaneously or may vary over time from one form to another in the same patient.[6]

Some studies[4,7,8] show that OLP may have malignancy potential for Oral Squamous Cell Carcinoma (OCC), with erosive and atrophic types having a higher incidence of malignant transformation. The estimated frequency of this event can vary from 1 to 5%, but there are still controversies due to variations between different publications.[5,7,8]

It is important that histopathological analysis is performed both to confirm the correct clinical diagnosis and to rule out the appearance of dysplasia and malignant transformation, although often only the clinical characteristics associated with the anamnesis are sufficient to make a possible diagnosis of OLP.[9]

Because it is a mucocutaneous disease, OLP can cause extraoral lesions that will affect the skin, glans penis, nails, scalp, esophageal and vaginal mucosa; intra-oral lesions are usually located on the bilateral buccal mucosa, dorsum of the tongue and gingiva, highlighting the need for multidisciplinary care.[10]

Despite occurring in various regions of the body, the oral cavity is often the first site of appearance, and in some cases it is the only form of presentation. With this in mind, it is possible to perceive the importance of the dental professional performing a correct diagnosis so that he can proceed with the appropriate therapy.[5]

Studies show[11,12,13] that stress, anxiety and depression are factors that can cause physiological changes in the immune system. Due to the increase in the number of people suffering from emotional disorders, the involvement of OLP can intensify, as troubled mental conditions tend to cause changes in the neuroendocrine system, thereby compromising the individual's immune function, leaving more susceptible to infections and diseases. autoimmune diseases, in addition to contributing to the perpetuation of inflammatory diseases.[11,12,13]

The review intends to show the importance of knowing how to identify and differentiate the types of OLP, in order to carry out an adequate and efficient treatment; guide people to seek dental care at the beginning of signs and symptoms in order to prevent the advancement and worsening of the disease, making treatment faster and simpler. The present study aims to show through a literature review the diagnosis of Oral Lichen Planus, review its etiology, its various clinical forms and address the most recent treatments available.

METHODS

Books and scientific papers on the topic were revised and online databases such as Scielo, PubMed, Lilacs and Google Scholar were searched. Papers published in English and Portuguese language were included.

The search terms in Portuguese and English were: Lichen Planus, Lichen Planus, Oral Pathology, Oral Mucosa, Corticosteroids, Corticosteroids.

LITERATURE REVIEW

In 1869, physician Erasmus Wilson first described a chronic dermatological pathology, which he believed to be mediated by the immune system and frequently affected the oral mucosa, this pathology was called Lichen Planus.[14] The term Oral Lichen Planus is used when the disease occurs in the oral cavity, characterized as a chronic inflammatory disease, immunologically mediated, affects mainly women, and usually occurs between the fourth and fifth decade of life. In addition to the oral cavity, it can affect the skin, scalp, nails, esophageal mucosa and vagina, and when in men, it can also affect the penile glans. Despite affecting other regions, the oral cavity is usually the first site of appearance of OLP, being in some cases its only form of manifestation.[15]

Etiology and Pathogenesis

Nowadays, the etiology of OLP remains unknown, however, it is believed that some external and internal factors may be associated with its development, such as viruses (Hepatitis C), drugs, restorative materials (amalgam), genetic predisposition and psychological disorders. [16] Although the etiology is unknown, its pathogenesis is well explained and studies show that cytotoxic T lymphocytes induce apoptosis of keratinocytes of the basal layer, leading to the development of a chronic inflammatory process.[17,18]

Emotional factors such as stress, anxiety and depression cause changes in the neuroendocrine system which is responsible for the production, distribution and release of hormones in the body, which can cause physiological changes in the immune system, leading to the development or worsening of autoimmune diseases such as OLP.[19]

Oral Manifestations

When present in the oral cavity, the disease is characterized by white streaks on the mucosa, white plaques or papules, atrophic, vesicular or atrophic-erosive lesions. The most affected sites are the lips, dorsum of the tongue and buccal mucosa. According to the literature, OLP can present six classic clinical forms: reticular, erosive, atrophic, plaque, papular and bullous.[20]

Reticularis is the most common clinical aspect, it presents as a pattern asymptomatic white striae, known as Wickham's striae, occurs bilaterally and in some cases affects the posterior mucosa of the buccal mucosa and lips. The reticular type has no symptoms.[21] The erosive type is the most severe form of the disease, manifesting symptomatic lesions surrounded by fine radiating keratinized streaks with a mesh appearance. It can range from simple discomforts to episodes of intense pain, which can cause changes in the patient's masticatory function when ingesting hot, acidic and spicy foods. [4,20]

The atrophic form manifests itself with the appearance of symptomatic diffuse red lesions, it generally resembles the presence of two clinical forms: white streaks characteristic of the reticularis, surrounded by an erythematous region. The gingiva may present erythema or ulcers and because of the similarity with gingival inflammation it is called desquamative gingivitis.[4,22]

The plaque type presents whitish homogeneous irregularities, similar to leukoplakia. Plaques have multifocal distributions and can be raised, smooth, and slightly irregular. They usually involve the dorsum of the tongue and buccal mucosa, often have no symptoms and do not require specific treatment.[20]

Papular, is a form observed sporadically and is usually followed by another type of variation. It has small white papules that vary in size between 1.0 mm and 0.5 mm, with fine striations on the surface.[20] And finally there is Bullous Lichen Planus, it is the most uncommon aspect of the disease, it occurs when the

erosive type is very severe, with this, the separation of the epithelium occurs, resulting in blisters. It usually has a short duration, manifests blisters that can vary from small millimeters to centimeters and tend to rupture, leaving the lesion ulcerated and painful. It is frequently found on the posterior buccal mucosa, in the region of the 2nd and 3rd molars.[23]

Diagnosis

The diagnosis can usually be made only by the clinical findings associated with the anamnesis, however, it is important that a histopathological analysis be performed, such as biopsy with direct immunofluorescence analysis, both to confirm the correct clinical analysis and to rule out the appearance of dysplasias and malignant transformation.[24]

In cases where the patient has candidiasis, the clinical diagnosis may be more difficult, since the microorganism can modify the specific reticular pattern of OLP, so, for a correct histopathological interpretation, the infectious condition needs to be previously treated with antifungal agents.[9, 24]

Differential Diagnosis

Histopathological examination, such as biopsy with direct immunofluorescence analysis, should always be performed, as OLP can be related to other diseases and alterations such as candidosis, leukoplakia (mainly of the proliferative verrucous type), cicatricial pemphigoid, pemphigus vulgaris, erythroleukoplakia, lupus erythematous, and chronic ulcerative stomatitis.[25]

Potential of LPO to become malignant

According to the World Health Organization (WHO), OLP has the capacity to become malignant[26], but it is still a much debated subject in the literature, generating much controversy. The oral cavity is exposed to several external and internal factors that can cause inflammatory stress, and make the mucosa vulnerable to inflammatory and infectious processes, such as those present in OSCC. The erosive form is the most favorable for malignant transformation, due to its characteristics.[27]

Some Studies[3,15,28] associate inflammatory stress predisposing cancer to some factors such as infection, alcohol, tobacco, location, advanced age, genetic predisposition, clinical form of OLP. Although there are doubts about the possible malignancy of OLP, some literatures state that lichen planus can indeed lead to the development of CCEO, although low.[3,15,28]

Whether or not it has the potential to become malignant, it is very important that when affected by the disease, follow up with the dentist for monitoring and for early detection of some changes that may indicate a malignant development.[14]

Recent concepts in treatments

OLP is a pathology that currently has no cure, its treatment tends to minimize the symptoms of the disease and extend its period of remission. Before starting any method to treat it, it is important to carry out a thorough clinical examination in order to eliminate possible irritating or aggravating local factors present in the oral cavity, such as sharp edges of restorations, fractured teeth and harmful habits. In addition, consumption of irritating foods and drinks, tobacco and alcohol should be avoided. Patients with the reticular type or other asymptomatic lesions did not require any other treatment.[19]

OLP therapy is aimed at decreasing symptoms and prolonging periods of pathology relief, complete eradication is currently not possible, there are a variety of treatments suggested, however, there is no strong evidence of their effectiveness. The first treatments available for OLP included the use of topical calcineurin inhibitors and topical systemic corticosteroids. Recently, studies have shown the use of low-level lasers and ozone therapy, used adjuvants to drug therapy, where it was possible to observe excellent results in reducing the signs and symptoms of the disease.[6,19,29]

The treatment of OLP can be divided into pharmacological and non-pharmacological. Pharmacological therapy has been the mainstay for the treatment of OLP, resulting in the use of calcineurin inhibitors and corticosteroids. On the other hand, non-pharmacological therapy has been used more recently and consists of the

application of ozone therapy and low-level laser.[15,30]

Pharmacological Therapy

Corticosteroids

Endogenous glucocorticoids are hormones produced naturally by the human body, called cortisol, it is synthesized by the adrenal gland, they are involved in various physiological functions and adaptation to stressful situations, being essential for life. Currently on the market, exogenous glucocorticoids are the most effective to obtain an anti-inflammatory and/or immunosuppressive action, however, prolonged use can cause a series of adverse effects, among which hematological alterations stand out, leaving the individual more susceptible. to other infections, adrenal insufficiency, and Cushing's syndrome.[31,32,33]

Corticosteroids are used as the first-choice therapy in the treatment of OLP, their administration can be topical and/or systemic. Topical administration is generally the most used, as it has a lower ability to cause adverse effects. The most used topical corticosteroids are: Triamcinolone Acetonide 1mg/g – ointment, preferably apply at night for 7 days, Clobetasol Propionate 0.5 mg/g – ointment, apply 12/12 hours for up to 4 weeks. If the symptoms continue after the prescribed days, discontinue use and seek the doctor or dentist to carry out a new evaluation, as the prolonged use of topical corticosteroids can also lead to an insufficiency of the adrenal glands, causing an insufficient production of cortisol or tachyphylaxis which consists of a decrease in its biological efficacy.[10,15,34,35]

The only disadvantage of topical corticosteroids is their lack of adhesion to the mucosa for a long time, adhesive pastes such as sodium carboxymethyl cellulose (Orabase) can be used together to promote good adherence of the ointment or in cases of lesions in the gingival region or the palate, custom-made trays can be made, which will ensure that the entire injured surface is exposed to the drug for the necessary period. Pseudomembranous candidiasis is the only side effect of the topical use of corticosteroids that can be prevented with the use of antifungals such as Miconazole gel or chlorhexidine-based mouthwashes concomitantly.[15]

Systemic corticosteroids will only be used in cases where the pathology affects other regions of the body or in severe cases such as the erosive and erythematous form, whose topical therapy has not been successful. The drug of choice in this case is Prednisolone, which should be prescribed at the lowest possible dosage for a shorter period, with 40 – 80 mg daily 12/12 hours being recommended for 5 to 7 days to avoid possible adverse reactions.[15,29,36]

Calcineurin Inhibitors

Another drug that has shown good results in the treatment of Oral Lichen Planus are calcineurin inhibitors. Calcineurin is a protein responsible for activating the transcription of IL-2, which is responsible for stimulating the growth and differentiation of T lymphocytes. Calcineurin is inhibited by calcineurin inhibitors, leading to a reduction in the activity or efficiency of the immune system, essential in treatments of autoimmune disease such as OLP. Inhibitors will reduce the number of T cells in the affected region and of inflammatory cytokines, as they also have anti-inflammatory effects. Cyclosporine, Tacrolimus and Pimecrolimus are the most used calcineurin inhibitors.[36,37]

Psychiatric Therapy

Emotional disorders can cause some changes in the neuroendocrine system, responsible for the production and release of hormones, which can compromise the patient's immune function, leading to the development or worsening of autoimmune diseases. With this, psychiatric therapy is very important for patients with OLP, because with the diagnosis the patient may experience more stress, anxiety and depression that can lead to periods of irritation from the disease. There are studies that show a reduction in the size and control of OLP lesions when using psychiatric drugs, increasing the period of remission of the diseases, so if you identify that the patient is suffering some kind of emotional disorder, you should refer him to a trained professional.[38,39]

Non-Pharmacological Therapy

Low-level laser therapy

Laser therapy is widely used in situations involving inflammatory reactions, need for tissue repair and pain. Photodynamic therapy has shown excellent results in the treatment of oral diseases such as OLP, with this, the use of this therapy is increasingly expanding, due to its numerous advantages, such as: minimally invasive, non-toxic, safe and low risk of complication and adverse effects.[31]

Several low-level lasers have been used for the treatment of OLP, including Helium-Neon (632 nm), ultraviolet (waves below 350 nm in length) and diode (red to infrared wavelength spectrum, 600 to 1100 nm). Each laser is used with different wavelengths, power, intensity, number of sessions, durations and therapeutic approaches.[40]

The laser that has been most used in this treatment is the diode laser, due to its easy access because it is marketed all over the world, easy to use and lower cost. Low-level laser is a great option in cases where only topical or systemic therapy is not effective or in cases where there are adverse effects of corticosteroids.[41,42]

The use of low-level laser therapy has been shown to be very effective in reducing symptoms, being even better when compared to corticosteroids, effective in reducing pain and regression of the pathology due to its analgesic and anti-inflammatory capacity, especially in cases of erosive OLP. In symptomatic cases of OLP, it is possible to obtain immediate relief in the first session after application, providing well-being and improving the quality of life of patients. Photodynamic therapy does not interact with the patients' systemic or topical medication, which makes it possible to use it in combination with corticosteroid therapy to obtain faster and better results.[41,43,44,45]

Ozone Therapy

Ozone is a highly unstable atmospheric gas that rapidly decays into normal oxygen, has an oxidizing capacity, produces only oxygen as a by-product, causing circulation to increase, increasing the amount of oxygen that reaches the tissues, tissue healing becomes better and faster. It also neutralizes the painful sensation by eliminating inflammatory mediators, has antimicrobial and antifungal action. Ozone can be used in three ways: gas, water and oil. Currently, due to lack of scientific evidence, ozone therapy should not be used in isolation, but associated with routine medication in order to accelerate the recovery process.[30,46]

The use of ozone therapy combined with topical corticosteroids as adjuvant therapy in cases of OLP has shown excellent results, reducing symptoms, controlling candidiasis infections due to its antifungal action and faster healing of the lesions. Ozonated water is the most used form in this treatment because it has a lower toxicity capacity when compared to gases that can be inhaled, this formulation allows reaching lesions located up to the oropharynx and can be a quick, safe and easy to use alternative. The half-life of ozone in water is approximately 10 hours, it is recommended in the clinical protocol that the mouth rinse be performed 5 to 10 hours after its production, in order to maintain its original concentration.[29,40,47]

Ozone has also shown great antifungal properties, the rate of candidiasis has been shown to be lower in the ozone-treated group. Thus, it can be concluded that the use of mouthwashes with ozonated water can be combined with topical corticosteroids as adjuvant therapy, resulting in safety and efficacy in the treatment of symptomatic OLP.[29]

Treatment with ozone therapy is a relevant proposal for stomatology, but it must be used in appropriate indications and concentrations. However, more research will be needed, as many of its effects have not yet been well clarified, in addition to not having a standardization of concentrations and doses for its application.[48]

FINAL CONSIDERATIONS

The etiology of OLP still remains unknown, however, there are several scientific evidences that prove that some factors can lead to its development such as the hepatitis C virus, medications, restorative materials such as amalgam, genetic predisposition and psychological disorders such as stress, anxiety and depression that can cause its onset or worsening.

In addition, it is known that its diagnosis can be made only by the clinical findings, associated with the anamnesis, however, it is very important to perform a histopathological analysis to confirm the

diagnosis and rule out the possibility of dysplasias due to the potential for malignancy.

Studies show that OLP can present six classic clinical forms, being reticular, erosive, atrophic, plaque, papular and bullous. Therefore, its treatment can be divided into pharmacological and non-pharmacological. The pharmacological treatment of first choice will be corticosteroids and as a second option, calcineurin inhibitors. The non-pharmacological treatment that has been used more recently will involve the use of low-level laser and ozone therapy, however, due to the lack of knowledge of the etiology, more studies should be carried out so that the treatment of the patient is increasingly assertive.

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