Treatment of denture stomatitis: literature review

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Abstract

Objective: this study aimed to investigate the main therapeutic options for denture stomatitis in patients using complete removable prostheses, to determine the best treatment method, avoiding relapses and improving patients' quality of life. **Material and Methods:** a search was made in the databases and electronic search tools PubMed, LILACS, SciELO and Web of Science using keywords, in Portuguese and English, such as denture stomatitis, *Candida albicans*, antifungal, oral candidiasis, and treatment. **Results:** studies have shown that the main drugs used in the treatment of denture stomatitis are miconazole, fluconazole, itraconazole, nystatin, amphotericin B, ketoconazole, clotrimazole and chlorhexidine. Regardless of the treatment employed, there is an improvement in the disease's clinical symptoms, but it does not prevent recolonization of the oral mucosa in patients with poor hygiene of the dental prosthesis. **Conclusion:** it is not possible to determine the best therapy for denture stomatitis, since the studies evaluated showed drug efficacy, but with relapses, especially in patients with poor hygiene of the dental prosthesis.

Keywords: Denture stomatitis; *Candida albicans*; Therapeutics.

Introduction

Denture stomatitis is one of the most common oral disorders of dental prosthesis users.[1] The etiology of denture stomatitis is multifactorial, and factors such as bacterial plaque accumulation, resin porosity, trauma caused by the use of inadequate prostheses and poor oral hygiene contribute to the mucosa underlying the prosthesis being susceptible to infection.[2]

This lesion affects about 65% of users of upper complete dentures. In addition, it is mainly observed in the palatine mucosa and most of the time it is asymptomatic, being able to present symptomatology, which includes pain, halitosis, pruritus, and burning.[3]

The diagnosis of denture stomatitis depends on clinical findings, such as, the presence of erythema and edema on the palatal mucosa and gingiva covered by the denture base.[4] In some cases, an association with candidiasis may occur, being essential the diagnostic confirmation. In presence of angular stomatitis or other systemic lesion further investigations are required, such as, blood picture, smears and culture, and biopsy of the lesion.[5,6]

After delivery of the complete dentures to the patients, orientation related to use, hygiene, and periodic monitoring is necessary to guarantee the functional conditions without presenting problems for the supporting tissues.

New therapies are being proposed for the treatment of denture stomatitis, through the use of natural products,[7,8] nanomaterials[9] and photodynamic therapy.[10] However, the treatment of choice for denture stomatitis consists, mostly of hygiene instructions of the prosthesis, of the application of a topical antifungal and verification of the need to make a new prosthesis.[11]

Although this lesion has been described for a long time, it is not defined yet what would be the best treatment, since there is a high number of relapse.

Therefore, the objective of this study was to review the literature on the primary therapeutic options.

Material and Methods

A search was realize in the databases and search tools PubMed Central, Latin American and Caribbean Center on Health Sciences (LILACS), Scientific Electronic Library Online (SciELO) and Web of Science using in isolation and/or combined the following keywords: denture stomatitis; *Candida albicans*; antifungal; antimycotic; oral candidiasis and treatment; in the Portuguese and English depending on the database. After reading the titles and abstracts, the articles of interest were selected and full texts acquired. There was no restriction regarding the year of publication and the type of study, and only articles published in Portuguese and English were included. Of the total of 98 articles found, only 54 were selected because they met the inclusion criteria for this review. This study sought to select at least one relevant article involving the use of each of the main antimicrobials used in the treatment of prosthetic stomatitis. Any unpublished data, letters to the editor and personal communications were excluded.

Literature Review

Candida albicans infection plays the most important role in the development of mostly of denture stomatitis.[3] Although the presence of this fungus in the mouth is regarded as commensalism, the transition from this condition to parasitism is related to an imbalance that occurs between the host and the fungus. Among these imbalance factors are: the continuous use of prostheses, trauma to the tissues due to inadequate occlusion, poor oral hygie-

ne, xerostomia, immunosuppression, HIV seropositivity, diabetes mellitus, endocrine and immunological disorders, and malignant diseases. This imbalance causes the fungus to promote the rupture of the protective barriers of the buccal mucosa.[12-14]

The etiology of stomatitis has a multifactorial cause. Once the functional and qualitative factors of the total dentures were isolated, they were insignificant for the occurrence of this disease.[15]

Stomatitis is identified by its clinical signs through the presence of petechiae or reddish areas in the region that is covered by the prosthesis.[3] In most cases, it is asymptomatic and, therefore, often goes unnoticed by patients, and is often discovered during routine oral exams. However, there are some cases in which the mucosa may be hemorrhagic and the patient may experience pruritus, burning, painful symptoms, unpleasant taste, halitosis and xerostomia.[16]

In most cases, the diagnosis of denture stomatitis is based on clinical signs and symptoms. However, when they are inaccurate, exams such as exfoliative cytology, culture, or biopsy may be useful in confirming the diagnosis.[17]

The prevalence of denture stomatitis in patients using removable prostheses is around 30-36%.[18,19] However, Lemos and Souza[3] and Maciel *et al.*[20] observed a much higher prevalence, of 59% and 78%, respectively. The prevalence of denture stomatitis is also associated with age, presenting a higher frequency in the age groups between 41 and 60 years.[18] There is a higher prevalence in females (84-86%).[20] However, Gauch *et al.*[19] did not observe a relationship between gender and denture stomatitis.

Due to the high prevalence of denture stomatitis, the participation of the dental surgeon is essential to controlling its triggering factors, and instruction on the use and cleaning of prosthetics is a prime factor.[21]

Denture stomatitis is associated with a lack of preventive hygiene programs, poor cleaning of dental prostheses and continuous use of dentures, not removing them to sleep.[22] It is believed that poor hygiene induce plaque/biofilm accumulation and, therefore, the growth of bacteria and fungi, making the mucosa vulnerable to denture stomatitis.[14]

Several mechanical and chemical methods, either isolated or associated, can be used to clean the dental prosthesis, such as: (1) brushing the prosthesis in running water; (2) brushing the prosthesis using a toothpaste; (3) brushing using ordinary soap; (4) cleaning with sodium hypochlorite (1.5-2.0%); (4) immersion in sodium hypochlorite (0.10-0.20%); (5) immersion in baking soda; (6) immersion in alkaline peroxide; (7) immersion in mouthwashes; and (8) use of effervescent tablets.[22-27]

The most important in the prevention and treatment of denture stomatitis is the quality of prosthesis cleaning and not the method used.[14,22] However, a combination of mechanical and chemical methods is considered the most appropriate choice in terms of denture cleaning, providing mechanical removal of biofilm and antimicrobial action.[23] In addition, a biannual examination is necessary for the evaluation of the prosthetic and the buccal cavity as prevention way to prevent and control the triggering factors.[11]

Vasconcelos *et al.*[28] proposed a protocol for prostheses and oral cavity hygiene. Participants received instruction on the use of prostheses, cleaning methods, shelf life, and the consequences of prolonged use. This protocol showed an improvement in the denture cleanliness index and a reduction in the prevalence of denture stomatitis. However, despite clinical improvement, it is often necessary to use antifungals to combat the pre-established disease. Therefore, the treatment of choice for denture stomatitis consists of the combination of antifungal, instruction regarding the importance of keeping the prosthesis clean, and verification of the need to change it. [11]

The antifungals most commonly used in the treatment of denture stomatitis are miconazole, fluconazole, itraconazole, nystatin, amphotericin B, ketoconazole, clotrimazole, and chlorhexidine.

Miconazole gel 2% is the antifungal that has been most successful in its application.[29] The medication is placed directly on the previously hygienized prosthesis which acts as a "tray" by giving the medicine more contact time with the lesions, thus promoting a better response and faster healing. This procedure should be done two or three times a day for one to two weeks. Only in cases in which there are no signs of improvement should systemic antifungal agents be used.[11]

Fluconazole (50 mg/day for 14 days) applied orally for treatment of denture stomatitis showed a positive response in 89% of patients, while no placebo patient responded positively to treatment. However, there were several degrees of relapse after four weeks of treatment. These results indicated that fluconazole is no more effective than topical treatment with other antifungal agents.[30] Martin-Mazuelos *et al.*[31] also showed a regression of clinical (97%) and microbiological (78%) signs after treatment with fluconazole. Patients who presented recurrence of the lesions underwent a new treatment with itraconazole at a daily dose of 100 mg for 18 days, resulting in a clinical and microbiological cure of 100% and 77%, respectively. Other studies also compared the action of fluconazole and itraconazole in the treatment of denture stomatitis, concluding that the two drugs were effective based on the reduction of palatal erythema and mycological culture.[24,32,33] However, in some cases recolonization by mi-

croorganism and persistence of the disease may occur.[25]

Another widely prescribed drug for the treatment of oral candidiasis is nystatin.[34] Topical application of nystatin 4 times/day for 15 days has proven to be effective in the treatment of denture stomatitis.[35,36] In addition, the simultaneous administration of suspension and tablets nystatin for two weeks resulted in a higher rate of clinical and mycological cure than did monotherapy.[37] Topical administration of nystatin in combination with amphotericin B also showed a significant clinical cure.[38] Finally, Falah-Tafti *et al*.,[39] when comparing the efficacy of nystatin and fluconazole in the treatment of denture stomatitis, concluded that nystatin is the standard topical treatment for oral candidiasis, with complete inhibition of the binding and colonization of *Candida albicans*. The rare presence of nystatin resistant fungi and its affordable cost are other advantages of this drug compared to other antifungals.[40]

Amphotericin B is also chosen for the treatment of denture stomatitis because of its acceptable taste, efficacy and low toxicity. It is considered a reference for the treatment of most fungal infections,[41] with excellent results against the strains of Candida albicans.[42] The evaluation of the efficacy of topical applications of amphotericin B in relation to systemic fluconazole showed that both were effective in the treatment of denture stomatitis. However, after 12 weeks, there was progressive mycological recolonization in both treatments.[43]

Ketoconazole is also an antifungal drug that has been frequently used to treat denture stomatitis, but its systemic use has some side-effects, such as poor appetite, nausea, vomiting, abnormal tiredness and/or fever.[42] Thus, Khozeimeh *et al*.[44] sought to evaluate the efficacy of topical ketoconazole 2% with systemic ketoconazole, concluding that both were effective, there was no significant difference between the two treatment plans, and topical medication has fewer side-effects, while systemic administration is associated with some complications.

Clotrimazole is a topical antifungal agent commonly used for the treatment of denture stomatitis associated with *Candida*. Czerninski *et al*.[45] compared the effectiveness of clotrimazole troches (5 troches of 10mg/day) with a clotrimazole varnish (50 mg/day) applied for 14 days. After the microbiological analysis, the results showed significantly lower levels of *Candida* in the saliva of patients who were treated with the varnish.

In addition to the systemic and topical applications of the above-mentioned drugs, mouthwash may also be use. In this respect, a chlorhexidine-based mouthwash merits attention.[27]

Chlorhexidine digluconate mouthwash (0.12%) was effective in eliminating *Candida albicans* from the dentures of patients with denture stomatitis.[27] Furthermore, chlorhexidine is effective against enzymes that are crucial in the pathogenesis of fungal infections.[46]

Candida albicans have a negative internal charge that explains their susceptibility to chlorhexidine.[47] The contact of *C. albicans* with chlorhexidine causes several cellular alterations, such as the fragmentation of the cell wall and the degeneration of the cytoplasm, resulting in the fungicidal effect of the drug.[27,48] In addition, chlorhexidine act in *C. albicans* by reducing phospholipase production, with cytoplasmic and nucleoprotein changes.[46]

An evaluation of antimicrobial action of drugs (nystatin, miconazole, ketoconazole, itraconazole, and chlorhexidine) incorporated in dentures on a *Candida albicans* biofilm showed that all antimicrobial agents were effective in inhibiting fungal growth.[49]

Among the new therapies proposed for the treatment of denture stomatitis, photodynamic therapy and the use of nanoparticles deserve special mention.

The studies have shown a positive effect of photodynamic therapy in the fight against denture stomatitis caused by *Candida*.[50-53] Methylene blue, toluidine blue and porphyrin derivatives have been the most commonly used photosensitizers.[10,51-53]

Nanomaterials have also been used in the treatment of denture stomatitis. Acosta-Torres *et al*.[9] developed poly(methyl methacrylate)-silver nanoparticle discs to prevent/treat denture stomatitis. The results show that nanoparticles discs significantly reduce the adherence of *C. albicans* and do not affect cell metabolism or proliferation, and their incorporation into dental prostheses is promising.

Among the articles evaluated on the therapeutic forms for denture stomatitis, it was observed that all antifungals have a significant treatment, some with greater clinical cure and others with greater mycological cure. A brief summary of the main treatment plans and the results can be seen in Table 1.

Table 1. Effect of antifungal drugs used in the treatment of denture stomatitis

Antifungal agent	Route of administration/treatment plan	Significance	Reference
Miconazole	Topical Gel 2%	Effective	(29)
Fluconazole	Oral 50 mg/day 14 days	Effective Relapse after 4 weeks	(30)
Fluconazole	Oral 50 mg/day 14 days	Effective Clinical cure (97%) Mycological cure (78%)	(31)
Fluconazole	Oral 50 mg/day 14 days	Effective	(24)
Itraconazole	Oral 100 mg/day 15 days	Effective	(24)
Itraconazole	Oral 100 mg/day 18 days	Effective Clinical cure (100%) Mycological cure (77%)	(31)
Itraconazole	Oral 100 mg 2 times/day 15 days	Effective Relapse in patients with poor hygiene	(25)
Itraconazole	Oral 100 mg 2 times/day 15 days	Effective	(33)
Nystatin	Topical 4 times/day 15 days	Effective	(35, 36)
Nystatin	Topical 1 month	Effective	(38)
Nystatin	Suspension and Tablets 14 days	Effective Clinical cure (87.5%) Mycological cure (66%)	(37)
Nystatin	Oral and Topical	Effective	(39, 54)
Amphotericin B	Topical 1 month	Effective	(38)
Amphotericin B	Topical	Effective Relapse after 12 weeks	(43)
Ketoconazole	Oral 200 mg/day 14 days	Effective	(44)
Ketoconazole	Topical Orabase 2% 2 times/day	Effective	(44)
Chlorhexidine	Topical Mouthwash (0.12%) 4 days	Effective	(27)
Clotrimazole	Troche 5 troches of 10 mg/day 14 days	Effective	(45)
Clotrimazole	Topical Varnish 50 mg/day 14 days	Effective	(45)

Conclusion

Based on the literature review, the treatment with all antifungal drugs proved to be effective with improvement in clinical and microbiological symptoms, but none of them prevented recolonization of the oral mucosa. Therefore, it is extremely important to identify predisposing factors. After installing removable prostheses, dental surgeons should be aware of the need for patient follow -up through of hygiene instructions of the prosthesis.

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Mini Curriculum and Author's Contribution

1. Karine Vitor Martins – DDS. Contribution: selection of articles, critical review of selected articles, and writing of the manuscript.
2. Sávio Morato de Lacerda Gontijo – DDS and PhD. Contribution: design of the literature review project, article selection, analysis and interpretation of selected articles, and writing of the manuscript.

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