

Denture Stomatitis

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Abstract: *Despite therapeutic progress, opportunistic fungal infectious diseases have increased in prevalence and becoming a universal and unresolved problem. Denture stomatitis is the most prevalent and long standing problem in denture wearers. The etiopathogenesis of denture stomatitis is multifactorial and complex to understand. The placement of denture produces significant changes in the oral environment and adversely affects the integrity of oral tissues. The combination of entrapment of yeast cells in irregularities in denture-base and denture-relining materials, poor oral hygiene and several systemic factors is the most probable cause for the onset of this infectious disease. Hence colonization and growth on prostheses by Candida species are of clinical importance. This article gives a comprehensive review of etiopathogenesis and management and current trends in management of denture stomatitis.*

Keywords: Denture stomatitis, Candida albicans, denture hygiene, antifungal drugs, photodynamic therapy, denture lining materials, dental plaque.

1. Introduction

Denture stomatitis (DS) also known as denture sore mouth and prosthetic stomatitis implies inflammation of the oral mucosa, especially palatal and gingival mucosa which is in direct contact with the denture base.¹ The prevalence of DS in edentulous patients has been reported as 62%, 39% and 23% respectively by different researchers.² No racial or sex predilection exists, although some authors have described a higher prevalence among women.³ Clinically the inflammation is of varying degrees and classifications, Newton's classification being most commonly accepted.¹ The condition is frequently symptomless, but when signs and symptoms are present they may display mucosal bleeding, swelling, burning or other painful sensations, halitosis, unpleasant taste and dryness in the mouth.⁴

2. Epidemiology

Denture stomatitis is a common condition: findings from several studies suggest that it can affect as many as 35-50% of persons who wear complete dentures. The prevalence of denture stomatitis among those wearing partial dentures is markedly lower than among complete denture wearers, whose rank goes from 10% to 70% depending on the population studied. No racial or sex predilection exists, although some authors have described a higher prevalence among women. This disorder is more frequent among elderly people, as they are more likely to wear removable dentures. However, there are reports that could not prove significant differences in the prevalence according to the age of the subject.⁵

3. Classification

It was first classified by Newton (1962) according to its clinical appearance as:

Type I: A localized simple inflammation or pinpoint hyperemia. Type II: An erythematous or generalized simple type seen as more diffuse erythema involving a part or the entire denture covered mucosa.

Type III: A granular type (inflammatory papillary hyperplasia) commonly involving the central part of the hard

palate and the alveolar ridges. Type III often is seen in association with type I or type II.

Type III denture stomatitis involves the epithelial response to chronic inflammatory stimulation secondary to yeast colonization and, possibly, low-grade local trauma resulting from an ill-fitting denture.⁶

4. Pathogenesis

Candida albicans has been shown to be the principal Candida strain responsible for inflammatory pathology, though various species of candida like C.dubliniensis, C. Parapsilosis, C. Krusei; C. Tropicalis and above all C.glabarta have been isolated from the inflammatory lesion.⁷ The pathogenesis of candida - associated DS is elaborate and multifactorial. C.albicans is a normal oral microorganism, and upto 67% of people carry this organism without clinical evidence of infection. Local and systemic factors can determine the transformation of C.albicans from a commensal to a pathogenic organism.⁸ The line between its status as yeast and hyphae is very thin and as the host cell becomes immunocompromised, it becomes active and starts secreting several hydrolytic enzymes such as proteinases and phospholipases which help in their adherence to host cells and digesting their cell walls for nutrient supply to assist further invasion.⁸

5. Predisposing Factors

The predisposing factors of denture induced stomatitis included systemic and local factors such as microbial factors, denture cleaning methods, wearing dentures through the night, ill-fitting denture, denture integrity (fracture, crack, hole...), poor oral hygiene and denture hygiene, xerostomia, smoking, quality and quantity of saliva, occlusion, parafunctional habits and carbohydrate rich diets, denture age and possibly a defect in host's defense mechanism.¹

5.1 Local Factors

Multifactorial findings

The etiology of denture stomatitis remains controversial as it is of multifactorial nature. Denture trauma, night time

denture wearing, denture cleanliness, dietary factors, Candida infections and predisposing systemic conditions have been proposed as associated factors in denture stomatitis.^(9,10,11)

Microorganism

It has been recently shown that the presence of *Candida albicans* in denture stomatitis is probably related to an extensive degree of inflammation¹² and that denture stomatitis is usually associated with the detection of *Candida* species while other factors such as denture hygiene habits¹³ and trauma⁴ are important to the development of the disease. The severity of the denture stomatitis has been correlated with the presence of yeast colonizing the denture surface.⁶ Dentures can produce a number of ecological changes that facilitate the accumulation of bacteria and yeasts. Bacterial proliferate: Certain bacterial species, like *Staphylococcus* species, *Streptococcus* species, species, *Fusobacterium* species or *Bacteroides* species has been identified in patients with denture stomatitis. *Candida* species, particularly *Candida albicans*, have been identified in most patients.³

Trauma

Nyquist considered traumas as the main liable to determine *Candida*-associated denture stomatitis with none association with the microbial communities and the presence of denture.¹⁴ Subsequently, Cawson showed that traumas and *Candida* infection are together responsible for the pathogenesis of the denture stomatitis. The latest study pointed out that trauma alone does not induce pictures of generalized denture stomatitis but, rather, it could be the cause of localized forms. Instead, in the generalized forms the principal pathogenetic role is played by *Candida albicans*. In this case, trauma could act as co-factor that favours the adhesion and the penetration of the yeast, sustains phlogosis of the palate and increases the permeability of the epithelium to toxins and soluble agents produced by *Candida* yeast. Denture trauma due to unstable dentures is also one of etiological factors of denture stomatitis. Immunohistochemical analysis of the mucosal tissue involved in denture stomatitis has demonstrated a possible role of trauma in the variation of expression of the basement membrane antigens.¹⁴

Denture lining material

Denture lining materials, which include tissue conditioners and soft denture liners, are widely used as adjuncts in the prosthodontic treatment and management of traumatized oral mucosa, and are most commonly used in association with the mandibular denture.⁴ Recently materials which are available are either silicone elastomers, plasticized higher methacrylate polymers, hydrophilic polymethacrylates or fluoropolymers.⁶ Even though these materials exhibit excellent tissue tolerance, one of the problems is the colonization of *Candida* species on and within the material. Fungal growth is known to destroy the surface properties of the liner and this may lead to irritation of the oral tissues. This is due to a combination of increased surface roughness and high concentrations of exotoxins and metabolic products produced by the fungal colonies.¹⁵

Denture plaque

Various microbiologic studies underlined that the plaque accumulated on the dentures during stomatitis has a complex composition, represented above all by Gram-positive bacteria,¹⁶ as *Streptococcus sanguis*, *S.gordonii*, *S.oralis*, *S.anginosus*, *Staphylococci* and rods as *Actinomycetes* predominately, followed by *Lactobacillus*. The microorganisms present in the oral cavity interact between them in various ways, as using directly their own metabolic products or exchanging themselves molecular signals. Several studies have shown that the coaggregation includes protein-carbohydrates interactions. *Candida* has been shown to be the predominant pathogen. First of all, it has been seen that patients with denture stomatitis show an increase in the presence of *Candida* when compared to the controls. Secondly, the patients response to the antimycotic therapy with a drastic decrease of the colonies present in the denture plaque. As third point, we must recall that the mass of yeast cell is 50 times greater than that of a coccus and that the mass of an hypha can be greater hundreds of times than that one of a rod. *Candida*, therefore, plays a key pathogenetic role in the onset of the denture stomatitis, even if the cooperative role practiced by the bacterial plaque present on the denture must not be neglected.¹⁷

Surface texture and permeability of denture

The tissue surface of the dentures usually shows micropits and microporosities. Such irregularities of surface make possible the yeasts to nest and make difficult to eliminate bacteria by mechanics and chemical hygiene manoeuvres; therefore, in presence of poor oral hygiene, *Candida* can penetrate, stick and aggregate with the bacterial communities.⁴ Substrate surface properties, as surface charge, surface free energy, hydrophobicity, and roughness have all been reported to influence the initial adhesion of microorganism.¹⁸ Penetration of the unpolished surface of the denture base, which is in contact with the mucosa, was greater than that of the polished surface. It was suggested that the unpolished surface of the denture was a suitable site for *Candida* proliferation and sealing of the surface was recommended.

The saliva

The role of the saliva in the colonization of *C. albicans* is still controversial. Some studies have shown that it reduces the adhesion of *C. albicans*. In fact, the saliva possesses defensive molecules as lysozyme, lactoferrine, calprotectin, IgA that decrease the adhesion of *Candida* to the oral surfaces.¹⁷ In other studies, it has been shown that salivary proteins as the mucines and the statherins may act as adhesion receptors used by the mannoproteins present in the *Candida* species.¹⁶ The decrease or the complete absence of saliva in individuals with xerostomy induces the change and the imbalance of the normal microbial communities favouring the proliferation of bacteria as *Staphylococcus aureus* that inhibits the normal adaptation of the commensals.¹⁶ Besides, the presence of a low level of pH and of a high oxygen tension reduces the growth of some commensals while increases the proliferation of *C. species*, *Streptococcus* mutants and *Lactobacillus*. Recent study show the saliva plays a dual role in the adhesion of *C. albicans* on plastic material used to make a dental prosthesis, decreasing

adhesion of germinated cell an enhancing the adhesion of yeast cell.¹⁹

pH of oral cavity

Low levels of pH can favour the adhesion and the proliferation of Candida yeast. In fact, a pH equal to 3 is optimal not only for the adhesion of the yeasts, but also for the enzymatic activity of the proteinases that, together with the lipases, are the most important factors of virulence of Candida because of their cytotoxic and cytolytic effects. Moreover, high levels of carbohydrates present in the saliva can act as an additional nourishing source for the Candida yeasts, that, by metabolizing these sugars, produce acid metabolic products and contribute to maintain low the environmental pH.¹⁶

Adhesion

The ability of Candida to pass through the tissues is the first step of the infectious process.^(20, 21) It has been observed that the forms endowed with hyphae are able to stick and to invade more quickly the tissues of the host. The complex mechanism of interaction between Candida and the host provides for the interaction between cellular ligands of Candida and cellular receptor of the host. The first ones consist in the mannoproteins present on the cellular surface. In fact the yeast produces extracellular polymeric material containing mannoproteins. The interaction with the epithelial cells happens between the mannoproteins and the fucose or the N-acetyl glucosamine present on the surface proteins of the epithelial cells.¹⁶

5.2 Systemic Factors

Certain systemic conditions such as diabetes mellitus, nutritional deficiencies (iron, foliate, or vitamin B12), hypothyroidism, immunocompromised conditions (HIV infection), malignancies (acute leukemia, agranulocytosis), iatrogenic immune suppressive drugs, e.g. Corticosteroids, may also predispose the host to candida-associated denture stomatitis.⁶

Diabetes

The saliva of diabetics favours the growth of C.albicans in vitro and it has been shown that on the denture surfaces of diabetic there are more elevated counts of colonies of the yeast by comparison with the non-diabetic subjects.²²

Deficiency of nutritional factors

Some authors report the sideropenic anaemia and high levels of cholesterol as causes of candidiasis.²³

Kidney affections

These affections are frequent in individuals of advanced age. The repeated treatments with antibiotics and sulphonamides can be predisposing factors because of the microbial alterations that they provoke in the oral cavity.²⁴

Xerostomy

Qualitative and quantitative alterations of the salivary flow in elderly patients are probably secondary to the assumption of drugs, above all the antihypertensive ones, rather than a primary functional deficit. Such reduction has been shown to act as predisposing factor to the virulence of the C. species.²⁵

6. Management and Preventive Measures of Denture Stomatitis

The treatment of Candida-associated denture stomatitis is complex because of its multi factorial etiology and depends upon a comprehensive plan. Elimination of predisposing factors is considered the first and most crucial step.²⁶ The therapeutic strategy still adopted includes the use of topical and systemic antifungal drugs, the use of preservatives and disinfectants, the irradiation with microwaves and the scrupulous removal and control of the plaque present on the denture and on the oral mucosa.⁷ Recent research has suggested the use of denture lining materials containing antifungals⁶ and the use of photodynamic therapy (PDT).²⁷

Correction of ill-fitting denture

Ill-fitting dentures were considered to be the main predisposing factor for the occurrence of denture stomatitis. Therefore, improving adaptation of the denture should be considered for the management of denture stomatitis.⁶ Correction of ill-fitting denture is considered important for the treatment of denture stomatitis.⁵ Discontinuous denture wearing are also considered important for the treatment of denture stomatitis.

Antifungal agents

The antifungal treatments more used are antifungal suspensions based on nystatin, amphotericin-B, miconazole and fluconazole. Almost all drugs generally produce a complete remission of symptoms within 12-14 days. Webb says that Epstein et al. showed the importance of antifungal therapy in the treatment and prevention of oral candidiasis.²¹ They noticed that nystatin and amphotericin-B, because of their binding to the ergosterol on the Candida cellular membranes, causes changes in the permeability of the cell membrane, leading to their penetration into the cells and causing finally the cell death. Tobudic et al.²⁸ bring that Merkel and Phelps showed that sub-lethal doses of amphotericin-B inhibits the adhesion of Candida to the cultures of mammalian cells, and that the blastospores in the stage of active growth are more sensitive to the drug. Other studies have shown that sub-inhibiting doses of nystatin, amphotericin-B and miconazole inhibit adhesion of Candida to epithelial cells.²⁸ Among the topically antifungal drugs used, the efficacy of "locetar" was noted;²⁹ it is used in the treatment of onychomycosis. Amorolfine belongs to a new class of chemical antifungal. It's fungistatic and fungicide effect is based on the alteration of the fungal cell membranes, in particular at the level of the sterols biosynthesis. In this way, the content of ergosterol is reduced, and at the same time not usual planar sterols accumulate. Amorolfine possesses a broad spectrum of action in vitro, and it is particularly effective versus dirofilariosis (trichophyton, microsporum, epidermophyton), yeasts (Candida), moulds (Alternaria, Hendersonula); with the exception of Actinomycetes, the bacteria are not sensitive to amorolfine.

Topical antifungals

Topical antifungal therapy for oral candidal infections is available in many forms like pastilles, troches, creams, ointments and oral suspensions and remains the cornerstone of treatment in mild, localized cases of candidoses in healthy

patients.³⁰ It was shown that most *Candida* species are susceptible to topical antifungal drugs like amphotericin B,^(31,31) nystatin,²¹ Miconazole^(33,34,35,36) and clotrimazole.³⁷ Being recommended as the first choice of treatment,³⁷ Amphotericin B is usually in the form of lozenges or oral suspension, while nystatin can be in the form of cream, pastille and oral suspension. On the other hand, clotrimazole is usually presented in a cream or solution form; the cream form also has an antistaphylococcal activity.³⁷ Miconazole can be used as a lacquer,^(34, 38) gel^(32, 36) or cream. The gel form of miconazole was shown to be more effective than the lacquer form.³⁶ Chlorhexidine in the form of mouth wash (0.2%) and 2% suspension for overnight denture disinfection can also be used to supplement antifungal drugs.³⁹

Systemic antifungals

Systemic antifungal agents have been recommended for patients with poor compliance such as patients with special needs. They are also recommended for immunocompromised patients.⁴⁰ Among systemic antifungal drugs, fluconazole and itraconazole have been the most extensively studied and proven as efficient antifungal drugs.^(41,42) Specifically, fluconazole is one of the most effective agents for the treatment of oropharyngeal candidiasis in HIV-infected patients as well as prophylaxis for fungal infections in neutropenic patients undergoing bone marrow transplantation.^(43,44) It was shown to be effective, especially when administered with an oral antiseptic such as chlorhexidine.⁴⁵ Compared to miconazole, it was demonstrated that fluconazole is more effective.³⁵ It is the drug of choice in the management of HIV-related oral candidiasis and it is superior to other topically administered or systemic antifungals due to its water solubility, oral bioavailability and good safety profile.⁴⁶ Fluconazole is usually used in the form of 50 or 100 mg capsules. However, it should be given with caution in certain circumstances as it interacts with anticoagulants among other drugs. It is also contraindicated in pregnancy and liver and renal disease. Itraconazole also was shown to be effective in the management of DAS,⁴² and even more effective than fluconazole.⁴¹ Martin-Mazuelos et al., (1997) showed that itraconazole was effective against 100% of fluconazole resistant strains.⁴⁷ Similar to fluconazole; it is usually used in the form of 100 mg capsules.

Preservative and disinfectant agents

The use of antiseptic substances as the 0.2% chlorhexidine gluconate administered 3 or 4 times a day, is capable of carrying on a significant reduction of the plaque but it has not a significant effect on the reduction of the colonies of *Candida*.²¹ More encouraging results are obtained when the dentures are immersing into 2% chlorhexidine as aid to topical therapy. Note that the chlorhexidine never must be administered at the same time with the nystatin since it inhibits the antifungal capacity. Another antiseptic substance used is sodium hypochlorite. It is proven that by diving the denture in a solution of 0.02% sodium hypochlorite, the number of *Candida* and bacteria amount on the denture surface effectively decrease. Unfortunately, sodium hypochlorite may not be used for an indeterminate period of time according to its ability to damage the prosthetic handiwork.⁴⁸

Microwave irradiation

Irradiation with microwave has been proposed as a quick effective and cheap method for the denture disinfection. In vitro the exposure to the microwaves was able to cause the cell death of *Candida albicans*.⁷ There are many evidences showing a new alternatives, such as the use of microwave irradiation at a specified setting and exposure time, are bactericidal and fungicidal.⁴ Thomas and Webb⁴⁹ demonstrated that microwaving of dentures at medium setting (350 W, 2450 MHz) for six minutes caused minimal change which was considered to be harmless in the long-term.

Scrupulous removal of denture plaque

The poor oral and denture hygiene are fundamental in the onset of disease, demonstrating the importance of the cleanliness of the denture through mechanical and chemical methods.⁵⁰ An efficient control of the microbial plaque on the denture remains the most important and certain procedure to follow. A good oral hygiene can be alone effective in treating denture stomatitis as well as when it is adopted in association with systemic and topical antifungal drugs. The hygiene control of denture is also essential to avoid relapses of pathology following treatment with antifungal drugs and, therefore, it is an important measure for the prophylaxis of candidiasis. Both the prosthesis that oral mucosa in contact with it must be involved in procedures for oral hygiene through brushing them after each meal with water or chemical agents. The patients should also be instructed to remove the denture during night and to leave it dry; in addition, during therapy for stomatitis, the prosthesis should be removed for at least two weeks.

Surgical treatment

In mild cases of inflammatory papillary hyperplasia antifungal treatment without surgery might be an alternative before the dentures are relined or replaced. In severe papillary hyperplasia of palate, cryosurgery or excision can be considered.⁶

7. Recent Studies in Management of Denture Stomatitis

A number of in vitro and in vivo studies have been carried out by incorporating antifungal agents into denture lining materials and were shown to be more effective and preventive against denture stomatitis. Several attempts have been made to incorporate antifungal agents such as propolis,⁵¹ zeolite,^(52,53) chlorhexidine,⁵⁴ punica granatum,³³ Nystatin,^(55,56) Fluconazole,⁵⁴ Itraconazole,⁵⁶ Miconazole,⁵⁷ Ketoconazole,⁵⁷ Clotrimazole⁵⁸ in the resilient liners with varying degree of success. Photodynamic therapy (PDT) appears to be a promising method of treatment compared with antifungal agents. A study conducted by using PDT was shown to be an alternative method of treatment for DS.²⁷ Recent study showed that the prevalence of denture stomatitis is reduced when mandibular dentures are stabilized by implants and concluded that implant over dentures could be an effective in controlling denture stomatitis by preventing trauma to the oral mucosa in edentulous elders. Better maxillary oral mucosal health may result when mandibular dentures are supported by minimum of two implants.¹⁴

8. Conclusion

This article reviews the etiopathogenesis and various approaches of preventive and management aspects of denture stomatitis. Though candida albicans was thought to be the principal cause in the etiology of DS, it may not be present in all cases. Hence it is important not to prescribe antifungal drugs without mycological investigations. As DS is generally asymptomatic; patients wearing dentures should be examined periodically

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