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ORAL CANDIDIASIS: A REVIEW

Dr. Pratik Parkarwar^{1*}, Dr. Venkatesh Kawaldar², Dr. Rupali V. Mhaske³ and Dr. Avanti Murarkar Vyas⁴

¹Reader, Department of Oral Medicine and Radiology, PDU Dental College Solapur, Maharashtra, India, PhD Scholar Department of Oral Medicine and Radiology. CSMSS Dental College and Hospital, Chhatrapati Sambhaji Nagar, Maharashtra, India.

²Assistant Professor. Department of Public Health Dentistry. PDU Dental College. Solapur. Maharashtra, India.

³Assistant Professor, Department of Oral Medicine and Radiology, CSMSS Dental College and Hospital, Chhatrapati Sambhaji Nagar, Maharashtra, India. PhD Scholar in RDDC Nagpur, Maharashtra, India.

⁴Tutor, Dept. Of Pedodontics, PDU Dental College, Solapur, Maharashtra, India.

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***Corresponding Author: Dr. Pratik Parkarwar**

Reader, Department of Oral Medicine and Radiology, PDU Dental College Solapur, Maharashtra, India, PhD Scholar Department of Oral Medicine and Radiology. CSMSS Dental College and Hospital, Chhatrapati Sambhaji Nagar, Maharashtra, India.

ABSTRACT

Candidiasis is a universal opportunistic fungal infection of the oral cavity which may be a reason of distress in dental patients. The article reviews common clinical types of candidiasis, its diagnosis, current treatment modalities with stress on the role of deterrence of repetition in the susceptible dental patient. The dental hygienist can play a vital role in education of patients to avoid recurrence. The incidence of invasive fungal infections (IFIs) has amplified over the last decade with the ascend in at-risk populations of patients. The morbidity and mortality of IFIs are high and management of these conditions is a great dare. With the extensive adoption of antifungal prophylaxis, the epidemiology of invasive fungal pathogens has altered. Oral candidiasis is a familiar fungal infection in patients with an impaired immune system, such as those undergoing chemotherapy for cancer and patients with AIDS. The systemic azoles, ketoconazole, fluconazole and itraconazole, have been a main advantage in treatment. To date, confrontation has mainly been a problem with fluconazole in AIDS.

However, it is important that measures are instituted to prevent the spread of defiant strains and the development of cross resistance.

KEYWORDS: Candidiasis, Opportunistic, CD4, Azole, IFI.

INTRODUCTION

Oral candidiasis is one of the most common, treatable oral mucosal infections seen in persons with human immunodeficiency virus (HIV) infection.^[1] Oral candidiasis can be a frequent and significant source of oral discomfort, pain, loss of taste, and aversion to food. *Candida albicans* carriage and a history of oral candidiasis are other significant risk factors for oral candidiasis.^[2] The infection is caused by *Candida Albicans*, a dimorphic fungal organism that typically is present in the oral cavity in a nonpathogenic state in about one-half of healthy individuals. Normally present as a yeast, the organism, under favorable conditions, has the ability to transform into a pathogenic hyphael form. Conditions that favor this transformation include broad-spectrum antibiotic therapy, xerostomia, immune dysfunction, or the presence of removable prostheses. Furthermore, about one in four patients with lichen planus will have superimposed candidiasis. This superficial nature of the infection makes oral candidiasis so amenable to treatment. Several antifungal agents can be used topically. For topical agents, successful therapy depends on adequate contact time (2 minutes) between the agent and the oral mucosa. Treatment duration varies from 7 to 14 days, with therapy minimally continued for 2 to 3 days beyond the last clinical signs and symptoms. Topical agents have the benefit of few side effects at normal therapeutic doses because of their lack of gastrointestinal absorption.

However, sucrose containing topical agents can be cariogenic when used over prolonged time periods, such that adjunctive topical fluoride therapy may be needed. Systemic antifungals have the advantage of once-daily dosing and simultaneous treatment of fungal infections at multiple body sites. However, these antifungals have more side effects, and selection requires consideration of important drug interactions. The present work reviews the common clinical types of oral candidiasis, its diagnosis, and current treatment modalities with emphasis on the role of prevention of recurrence in the susceptible dental patient. The dental hygienist can play an important role in the education of patients to prevent recurrence. Candidiasis is a common oral and perioral opportunistic infection that usually results from overgrowth of endogenous *Candida* fungal microorganisms. There are many species of *Candida*^[3, 4] but *C. albicans* is the fungal microorganism most often encountered in the ambulatory general

practice dental patient. Changes in the oral environment that can predispose or precipitate oral candidiasis include: antibiotics, corticosteroids, dry mouth (xerostomia), diabetes mellitus, nutritional deficiencies, and immunosuppressive diseases and therapy. Saliva contains antifungal proteins including histatins and calprotectin that help protect patients from *Candida* infections.^[5] These protective proteins are absent in a patient who has xerostomia. Individuals who use corticosteroid asthma inhalers must rinse their mouths with water after each use to reduce their chances of developing oral candidiasis.

Excellent oral hygiene, including brushing and flossing of the teeth twice daily and maintenance of adequate intraoral moisture, is critical in the prevention of candidiasis recurrence in the susceptible patient. Fluconazole, a novel bis-triazole antifungal agent introduced in 1990, has systemic effects that may be beneficial for other fungal infections. Subjects in the fluconazole prophylactic arm of one antifungal placebo-controlled trial showed improvement of dermatophytoses, such as tinea pedis, onychomycosis, and tinea cruris.^[6] In addition, systemic fluconazole prophylaxis may prevent esophageal and vaginal candidiasis^[7], cryptococemia, histoplasmosis, and other deep fungal infections. Unlike ketoconazole, fluconazole is not altered by changes in gastric acidity and carries less risk of hepatotoxicity; however, many of the same drug interactions are possible. A newly raised concern about the wide spread use of fluconazole is the potential for development of azole-resistant *Candida albicans* and selection of nonalbicans *Candida* species, which also increase in prevalence with immune decline and further complicate management of some individuals.^[8,9,10]

Causative organisms

Candida

Species of Oral Candida

1. *C. albicans* 5. *C. parapsilosis*
2. *C. glabrata* 6. *C. pseudotropicalis*
3. *C. guilliermondii* 7. *C. stellatoidea*
4. *C. krusei* 8. *C. tropicalis*

Among the fungal pathogens, *Candida* spp. is the most predominant causes of invasive infections. *Candida glabrata* infections are rare in infants and children but are significantly more common in the elderly.^[11]

Candida tropicalis plays an important role as a cause of invasive diseases in patients with haematological malignancy.^[12] Overall, the non-albicans *Candida* spp. have shown an increasing trend as causative pathogens in BSIs.^[13] However, the role of species with lower susceptibility to azoles has been limited in other areas. New triazoles, such as voriconazole and posaconazole, and the echinocandins are active against these two species, although cross-resistance was noted within the azoles in some *C. glabrata* strains.

Aspergillus spp

Aspergillus spp. is commonly found in soil, water and decaying material all over the world. Unlike invasive candidiasis, invasive aspergillosis (IA) occurs predominantly in highly immunocompromised patients.^[14, 15, 16] The main affected populations are patients with Haematological malignancies and/or those receiving haematopoietic stem cell transplantation (HSCT).^[17] IA is also an emerging condition in patients with other causes of immunosuppression, such as solid organ transplantation, advanced acquired immunodeficiency syndrome (AIDS) and treatment with newer immunosuppressive agents such as infliximab.^[18] The usual route of infections for IA is inhalation of *Aspergillus* conidia. The most frequently involved sites of IA are sinuses, lungs, brain and disseminated infection.

Other moulds

Zygomycetes are fungi belonging to the order Mucorales, which form broad hyphae and are generally non-septate. Genera that are able to cause invasive diseases include *Rhizopus*, *Rhizomucor*, *Absidia* and *Cunninghamella*.^[19, 20] Infections due to zygomycetes are classically characterised by vascular invasion, leading to thrombosis and tissue necrosis. Zygomycetes are susceptible to amphotericin B but generally resistant to most triazoles and the echinocandins. Breakthrough zygomycosis has been reported in patients receiving voriconazole or caspofungin prophylaxis, as these agents lack activity against zygomycetes.^[21, 22] Voriconazole and posaconazole have been reported as successful treatments for fusariosis.

Clinical spectrum of the disease

Infection with *Candida Albicans* presents mainly in any of four forms:

Pseudomembranous candidiasis, Hyperplastic candidiasis, Erythematous candidiasis or angular cheilitis. Patients may exhibit one or a combination of any of these presentations.

Angular cheilitis, for example, will frequently be seen in combination with erythematous candidiasis in denture wearers.

Clinical classification

Pseudomembranous

Angular cheilitis

Chronic atrophic (erythematous)

Denture stomatitis

Endocrine-candidiasis syndrome

Hyperplastic (Candidial leukoplakia)

Inflammatory papillary hyperplasia

Median rhomboid glossitis

Mucocutaneous

Pseudomembranous candidiasis

Pseudomembranous candidiasis, commonly known as “thrush,” is the form often seen in neonates. It can also be seen in patients receiving topical corticosteroid therapy or in immune suppressed patients. In fact, the presence of pseudomembranous candidiasis in a seemingly healthy adult may be an indication of underlying systemic disease, such as infection with the human immunodeficiency virus (HIV). Pseudomembranous candidiasis presents as multiple white plaques of material resembling cottage cheese that can easily be wiped away.

These plaques consist of tangled aggregates of hyphae. The underlying mucosa may be erythematous, but ulceration would not be expected. While symptoms are typically mild for this form of infection, patients may complain of a slight tingling sensation or a foul taste. Identification of the fungal pseudohyphae within exfoliative cytologic preparations, often utilizing periodic acid Schiff and/or Papanicolaou stained preparations, is the optimal standard for the diagnosis of all candidiasis, although the highest yield of positive cytology smears is with pseudomembranous candidiasis.^[23]

Atrophic Candidiasis

Atrophic candidiasis exhibits a diffusely reddened, often relatively dry mucosa. The red areas are often confined to mucosa underlying dental appliances such as partial dentures or orthodontic retainers. Approximately 26% of patients with complete dentures have atrophic candidiasis.^[24]

Hyperplastic candidiasis

This form has been referred to as “candidal leukoplakia,” although this terminology should probably be avoided. Like leukoplakia, hyperplastic candidiasis will present as a white plaque that cannot be wiped away by the clinician. Unlike leukoplakia, however, lesions should completely resolve with routine antifungal therapy.

Erythematous candidiasis

Many conditions fall under the spectrum of erythematous candidiasis. As the term implies, lesions clinically appear red or erythematous. While any mucosal site may be affected, erythematous candidiasis commonly involves the tongue and palate. A form of erythematous candidiasis that is especially common involves the hard palate and gingiva beneath a denture or removable partial denture.

Angular cheilitis

The final clinical presentation of oral candidiasis infection is angular cheilitis. This form presents as cracking, peeling, or ulceration involving the corners of the mouth. It will frequently be seen in combination with one of the other forms of candidiasis infection, such as the erythematous type. Patients with a reduced vertical dimension of occlusion, secondary to severe attrition or worn dentures, are particularly susceptible to the development of angular cheilitis. This is due to the increased folding of the soft tissue that is frequently seen at the corners of the mouth, creating a haven for the organism.

Several over-the-counter (OTC) medications including miconazole nitrate and clotrimazole creams, and prescription nystatin or ketoconazole creams are available to topically treat angular cheilitis. Topical miconazole nitrate 2% cream is valuable in that it is effective against both *Candida* and *Staphylococcus aureus*. Dental professionals should be cautious when recommending OTC topical antifungals to patients who are using the anticoagulant warfarin. The combination increases the risk of excessively prolonged coagulation periods, due to interference with the liver enzymes that aid in the metabolism of warfarin.^[25] Angular cheilitis is typically clinically diagnosed based on the uni- or bilateral presence of asymptomatic or painful red cracks or fissures at the corners of the mouth. Angular cheilitis may be caused by candidiasis (20%), mixed candidial bacterial infections (60%), or bacteria alone (20%).^[26]

Treatment

For the normal healthy patient, the treatment of oral candidiasis is relatively simple and effective. Typically, topical medications are adequate. A commonly prescribed anti-fungal agent, nystatin oral suspension, will usually resolve most infections. However, topical medications must be in contact with the organism to eliminate it. Since patients are usually unable to hold liquids in their mouths more than briefly, clotrimazole troches are an effective alternative. These are dissolved slowly in the oral cavity, allowing the drug to be present for greater length of time.

Intraoral candidiasis

Topical agents include nystatin suspension and clotrimazole troches, which should be allowed to dissolve slowly in the mouth five times daily for 14 days. Patients should avoid eating or drinking for 20 minutes after using clotrimazole troches. Intraoral appliances should be removed during the treatment as the medication works topically and must be in contact with the tissue. Systemic prescription antifungal agents include ketoconazole, fluconazole, and itraconazole.^[27,28,29]

Prosthetic appliances

With any case of oral candidiasis, if the patient utilizes a removable prosthetic appliance it is important to disinfect the appliance, because the porous material or surface biofilm can serve as a reservoir of fungal microorganisms and contribute to relapse or reinfection.^[30] Disinfection of dental appliances is a two-step process. First, the appliance should be free of debris and concretions. Household chlorine bleach, although effective and inexpensive, can cause damage to dental metals, acrylic, and tissue-conditioning materials.^[31] To avoid damage to prosthetic appliances, a germicide deodorizer containing sodium benzoate, citrate, and disodium phosphate (Oral Safe, Great Lakes Orthodontics, Tonawanda, NY) can be used to soak the appliance for six hours. This solution can be reused for one week and is harmless if ingested.^[32] Another technique utilizes five minutes of microwave irradiation. Applying 60 Hz at full power to a complete acrylic denture in eight ounces of water can effectively sterilize acrylic and most soft denture liners.^[33]

Xerostomia

Such patients may require maintenance therapy of twice daily 0.12% chlorhexidine gluconate mouthrinses after an acute or chronic episode of oral candidiasis is under control.

Topical antifungal medications

Angular cheilitis

Miconazole cream 2%

Clotrimazole cream 1%

Ketoconazole cream 2%

Nystatin ointment 100,000 units/gram

Denture stomatitis

Nystatin topical powder 100,000 units/gram

Intraoral candidiasis

Nystatin oral suspension 100,000 units/gram

Clotrimazole troches 10 mg

Amphotericin B 100 mg/ml

Systemic antifungal medications

Ketoconazole tablet 200 mg

Fluconazole tablet 100 mg

Itraconazole tablet 100 mg

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