

Review Article

Oral Candidiasis: An Updated Review

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ABSTRACT

Oral candidiasis is one of the common fungal infections affecting the oral mucosa. These lesions are caused by the yeast like fungal organism *Candida albicans*. *Candida albicans* are one of the components of normal oral microflora and around 30% to 50% people carry this organism without clinical evidence of infection. Maintenance of oral hygiene and early diagnosis of this condition is very important. There are a few local factors that make the oral tissues susceptible to *Candida* infection. These include acidic saliva, xerostomia, night use of prosthetic dentures, tobacco, carbohydrate rich-diets and patients receiving radiotherapy and

chemotherapy in maxillofacial structures. The prognosis of oral candidiasis is good when the predisposing factors associated with this infection are eliminated. Maintenance of oral hygiene and early diagnosis of this condition is very important.

Keywords: Candidiasis, fungal infection, antifungal drugs.

Introduction

Oral candidiasis is one of the common fungal infections affecting the oral mucosa. These lesions are caused by the yeast *Candida albicans*. *C.*

albicans are one of the components of normal oral microflora and around 30% to 50% people carry this organism. Rate of carriage increases with age of the patient. *Candida albicans* are recovered from 60% of dentate patients' mouth over the age of 60years. It is said to affect very young, very old and the very sick individuals. Three general factors determining the clinical evidence of infection includes immune status of the host, oral mucosal environment and the strain of *C. albicans*. There are nearly six types of candida species which are seen in the oral cavity.¹

These are

- *Candida albicans*
- *Candida tropicalis*
- *Candida krusei*
- *Candida glabrata*
- *Candida parapsilosis*
- *Candida guilliermondi*

Among these five types, *Candida albicans* are commonly seen in the oral cavity. *Candida albicans* is a dimorphic fungus that causes severe opportunistic infections in humans.² An interesting feature of *Candida albicans* is its ability to grow in two different ways: reproduction by budding, forming an ellipsoid bud, and in hyphal form, which can periodically fragment and give rise to new mycelia, or yeast-like forms.³ Yeast is innocuous and hyphal forms are associated with invasion of host tissue. Strains with better adhesion potential are more virulent.

The main factors which increase the susceptibility to oral candidiasis are⁴

Local factors:

- Poor oral hygiene
- Smoking
- Inhalational steroids
- Atopic constitution
- Quality and quantity of saliva
- Dental prosthesis
- Hyperkeratosis

General factors:

- Immunosuppressive disease
- Malignancies
- Immunosuppressive drugs
- Hematinic deficiencies
- Infancy and old age
- Nutritional deficiencies
- Endocrine disorders

Xerostomia: Saliva contains IgA which inhibits binding of *Candida albicans* to mucosal surfaces. It also provides a flushing action which removes *Candida albicans* from oral cavity. In case of xerostomia both these actions are absent because of lack of saliva production, so chances of candidiasis is more in oral cavity. Xerostomia is also seen in case of anticancer treatment and irradiation which increases the proliferation of candidal cells and resistance of *Candida* cells to antifungal drugs. Xerostomia is also seen in case of Sjogren's syndrome.

Diabetes Mellitus: Growth of *Candida albicans* thrives on increased levels of glucose in saliva which increases the ability of *Candida albicans* to adhere to oral mucous membranes.

Medicines: Prolonged use of antibiotics depletes the normal oral flora and enables proliferation of

Candida albicans in the oral cavity. In asthmatic patients, the use of steroid inhalers, predisposes them to *Candida* infection. Steroid aerosols interfere with the normal balance of microflora and favour the proliferation of *Candida albicans*, whereas systemic steroids cause suppression of the immune system.

Classification: Oral candidiasis are mainly classified into primary and secondary infections.

I. Primary oral candidiasis⁴

Acute form

- i. Pseudomembranous
- ii. Erythematous

Chronic form

- i. Erythematous
- ii. Pseudomembranous
- iii. Plaque like
- iv. Nodular

Candida associated lesions

- i. Denture stomatitis
- ii. Angular chealosis
- iii. Median rhomboid glossitis

II. Secondary oral candidosis

Oral manifestation of systemic mucocutaneous candidiasis

- i. Familial mucocutaneous candidiasis
- ii. Diffuse chronic mucocutaneous candidiasis
- iii. Familial chronic mucocutaneous candidiasis
- iv. Chronic granulomatous disease
- v. Candidosis endocrinopathy syndrome
- vi. Acquired immune deficiency syndrome (AIDS)
- vii. DiGeorge syndrome
- viii. Severe combined immunodeficiency

Acute form of pseudomembranous candidiasis (also known as Thrush) affects patients under antibiotics,

immunosuppressant drugs, etc. the infection presents with loosely attached membranes. Clinically, there will be scrapable pseudomembrane formation with inflamed mucosa or bleeding area below. The chronic form may be due to HIV infection or in patients on steroid inhalers. It is seen as an erythematous surface with increased vascularization. The plaque type, earlier known as candidal leukoplakia, clinically presents with a white irremovable plaque formation. Both, the chronic plaque type and nodular type are associated with malignant transformation.

The pathogenetic theory in denture stomatitis states that the presence of bacteria such as Streptococci and Actinomycetes, induce the organism to produce proteases as IgA and enzymes such as aminopeptidases, hyaluronidase, chondroitinases and neuraminidases which enables the organism degrade the oral epithelium. The presence of these products, stored in close contact with the oral mucosa, determine an increase in the inflammatory exudate that favours the bacterial colonization and also the yeast proliferation, since *Candida* colonizes more easily on the mucosa in contact with the denture surface as compared to the rest of the buccal mucosa.

The proteases can increase the pathogenic potential of the bacterial substances, leading to the destruction of the salivary immunoglobulins. A delayed hypersensitivity reaction towards *Candida albicans* contributes to the inflammatory reaction and the exfoliation of the epithelial cells, leading to the epithelial atrophy. It is a typical feature of denture stomatitis. Denture stomatitis is divided into three clinical types. They are^{4,5}

- i. Type I - Localized pinpoint hyperaemia
- ii. Type II - Erythematous lesion involving denture covered mucosa

iii. Type III -Papillary type involving central part of hard palate & alveolar mucosa

These conditions are treated by antifungal drugs (Nystatin, Amphotericin-B, Miconazole and Fluconazole) and disinfectants (0.2% Chlorhexidine gluconate mouthwash 3 or 4 times a day), Microwave irradiation (exposure to the microwaves was able to cause the cell death of *C.albicans*) and scrupulous removal of denture plaque. Even though denture stomatitis is asymptomatic, it should be treated as it may act as reservoir for infections which can become extensive and lead to the resorption of the alveolar bone. The most effective treatment is the eradication and control of microbial plaque.^{6,7}

Diagnosis

Oral candidiasis is mainly diagnosed based on clinical sign and symptoms. Additional tests include:

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Exfoliative cytology

Culture

Tissue biopsy

ID – reaction: It is a secondary skin response which is a localised or generalized sterile Vesiculopapular rash. These rashes resolve with treatment.

Management: Always continue the treatment for two weeks after resolution of the lesions. If the topical therapy fails then one has to start systemic therapy because failure of drug response is the initial sign of presence of an underlying systemic disease. Follow-up appointment after 3 to 7 days is important to check the effect of drugs.

Main goals of treatment are:⁹

To identify & eliminate possible contributory

factors

To prevent systemic dissemination

To eliminate any associated discomfort

To reduce load of candida

Treatment options are mainly categorized into two lines, primary & secondary line of treatment.

Primary line of treatment: most commonly used antifungal drugs belong to the groups of polyene or azoles. Nystatin is the drug of choice as a primary line of treatment, other drugs include Clotrimazole which can be taken as Lozenges and Amphotericin B as oral suspension. These are well tolerated and are not associated with development of resistance.^{4,10}

Nystatin: It is used as a primary line of treatment. It is available as cream and oral suspensions. It is to be applied four times a day and allowed to act approximately for two minutes in the oral cavity and then swallowed. There is no significant drug interaction or side effects.

Amphotericin B: This drug is available as Lozenge (Fungilin 10mg) and oral suspension 100mg/ml which is to be applied 3 to 4 times daily after meals. Amphotericin-B inhibits the adhesion of Candida to epithelial cells. The side effect of the drug is nephrotoxicity.

Clotrimazole: This drug decreases fungal growth by inhibiting the synthesis of ergosterol. It is not indicated for systemic infection. This drug is available in Creams and Lozenge 10mg. it has antistaphylococcal activity also. Main side effects of this drug are unpleasant mouth sensation, increases liver enzyme levels, nausea and vomiting.

Second line of treatment:

The second line of treatment is used for severe, localized, immunosuppressed patients and patients who respond poorly to the primary line of treatment. Drugs mainly used in second line of treatment are:^{4,10}

- Ketoconazole
- Fluconazole
- Itraconazole
- Miconazole

Ketoconazole: It blocks ergosterol synthesis in fungal cell membrane and is absorbed from the gastro intestinal tract and metabolized in the liver. The dosage is 200-400 mg tablets once or twice daily for 2 weeks. Side effects are nausea, vomiting, rashes and pruritis, liver damage and also its interaction with anticoagulants. Contraindicated in pregnancy and liver disease.

Fluconazole: This drug inhibits fungal cytochrome P450 sterol C-14 alpha demethylation. It is used in oropharyngeal candidiasis and dosage is 50 – 100mg capsule once a day for 2-3 weeks. Main side effects are nausea, vomiting and headache. It interacts with anticoagulants and this drug is contraindicated in pregnancy, liver and renal disease.

Itraconazole: It is one of the broad spectrum antifungal agents and contraindicated in pregnancy and liver disease. The dosage of the drug is 100 mg capsule once a day for 2 weeks. The main side effects are nausea, neuropathy and rashes.

Miconazole: It is the treatment of choice for angular cheilitis often infected by *S. aureus* and candidal strains. It has biostatic effect on *S. aureus* in

addition to the fungistatic effect. It is available in the form of gel or cream and is applied 3-4 times daily.

Iodoquinol: not strictly an antifungal drug but has antifungal and antibacterial properties. In the cream form with corticosteroids is very effective for angular cheilitis.¹¹

Conclusion

The prognosis of oral candidiasis is good when the predisposing factors associated with this infection are eliminated. When the systemic predisposing factors arise even patients with primary candidiasis are at risk. In most of the cases oral candidiasis is a cause of secondary superficial infection which can easily be resolved with antifungal therapy.

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