

Topical Antifungals and Systemic Antifungals in the Management of Candidiasis

B Vivek Babu, Jayanth Kumar Vadivelu*
Department of Oral Medicine, Saveetha University, Chennai, India

ABSTRACT

INTRODUCTION

Candidiasis: A fungal infection typically on the skin or mucous membranes caused by candida.

Systemic antifungal: There are 3 main classes of systemic antifungals: the polyene macrolides (Amphotericin B), the azoles (the imidazoles Ketoconazole and Miconazole and the Triazoles itraconazole and Fluconazole) and the allylamines (Terbinafine).

Topical antifungal: Antifungal creams, liquids or sprays, These are used to treat fungal infections of the skin, scalp and nails. They include Clotrimazole, Econazole, Ketoconazole, Miconazole, Tioconazole, terbinafine, and amorolfine.

MATERIALS AND METHODS

A cross sectional retrospective study of, study population will 58 patients visiting Saveetha Dental College and Hospital with oral Candidiasis. Their antibiotic prescription was found. The data was tabulated and analysed. SPSS by IBM was used for data analysis.

RESULTS

Males were 69 % affected by candidiasis. Most common age group affected was from the age of 50 years to 60 years i.e 69 %. Clotrimazol was the most common antifungal used as topical antifungal i.e 98.3 %.

CONCLUSION

Males are most commonly affected. 50 to 60 years of age is the most common affected group. Clotrimazole is the most common topical antifungal used.

KEYWORDS

Candidiasis, Antifungal, Amphotericin B, Ketaconazole

Corresponding Author:

Vivek Narayan, Department of Oral Medicine, Saveetha University, Chennai, India. Email: jayanthkumar@saveetha.com

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INTRODUCTION

Oral candidiasis is an opportunistic infection of the oral cavity. It is common and under-diagnosed among the elderly population, particularly in those who wear dentures. It can also be the beginning of a systemic disease, such as diabetes mellitus and is a common problem among the immunocompromised individuals. Oral candidiasis is caused by an overgrowth or infection of the oral cavity by a yeast-like fungus, candida. The most common species are *C albicans*, *C tropicalis*, *C glabrata*, *C pseudotropicalis*, *C guilliermondii*, *C krusei*, *C lusitaniae*, *C parapsilosis*, and *C stellatoidea*. *C albicans*, *C glabrata*, and *C tropicalis* represent more than 80 % of isolates from clinical infection especially in early and later stages of life. *C albinos* are a normal commensal of the mouth and generally cause no problems in healthy people. Oral candidiasis is the most common human fungal infection.

There are a number of different types of oropharyngeal candidiasis including acute pseudomembranous, acute atrophic, chronic hyperplastic, chronic atrophic, median rhomboid glossaries, and angular chelates. The most discrete lesion represents conversion from benign colonisation to pathological overgrowth.

Pseudomembranous candidiasis (thrush) is characterised by extensive white pseudo membranes that consist of desquamated epithelial cells, fibrin, and fungal hyphae. These white patches occur on the surface of the labial and buccal mucosa, hard and soft palate, tongue, periodontal tissues, and oropharynx. The membrane can usually be scraped off with a swab to expose an underlying erythematous mucosa. Diagnosis can be confirmed microbiologically either by staining a smear from the affected area or by culturing a swab from an oral rinse. Predisposing factors include extremes of age, diabetes mellitus, patients who have HIV / AIDS or leukaemia, those using steroid aerosol inhalers, broad spectrum antibiotics, and psychotropic drugs. Other conditions that can give rise to white patches in the mouth are lichen planus, squamous cell carcinoma, lichen reaction, and leukoplakia.

Acute atrophic candidiasis is usually associated with a burning sensation in the oral cavity. The tongue may be bright red. Diagnosis may be difficult but should be considered in the differential diagnosis of a sore tongue especially in a frail older patient with dentures who has received antibiotic therapy or

who is on inhaled steroids. A swab from the tongue / buccal mucosa may give a better diagnosis.

Chronic hyperplastic candidiasis characteristically occurs on the buccal mucosa or lateral border of the tongue as speckled or homogenous white lesions. The lesions usually occur on the buccal mucosa or lateral borders of the tongue. There is an association with smoking and complete resolution appears to be dependent on cessation of smoking. This condition can progress to severe dysplasia or malignancy and is sometimes referred to as candida leukoplakia. *Candida sp* are not always isolated from lesions of oral leukoplakia and it has been suggested that the finding of *Candida spp* in these premalignant lesions is a complicating factor rather than a causative one. This condition may be confused with lichen planus, pemphigoid / pemphigus, and squamous cell carcinoma.

Chronic atrophic candidiasis also known as “denture stomatitis” is characterised by localised chronic erythema of tissues covered by dentures. Lesions usually occur on the palate and upper jaw but may also affect mandibular tissue. Diagnosis requires removal of dentures and careful inspection; swabs may be taken for confirmation. It is quite common with incidence rates of up to 65 % reported (Table 1).

AGE DISTRIBUTION	Frequency	Percentage
20 - 30	2	3.40 %
31 - 40	5	8.60 %
41 - 50	15	25.90 %
51 - 60	15	25.90 %
> 60	21	36.20 %

Table 1. Distribution between Age, Frequency, Percentage.

Median rhomboid glossaries are a chronic symmetrical area on the tongue anterior to the circumvallate papillae. It is made up of atrophic fusiform papillae. Biopsy of this area usually yields candida in over 85 % of cases. It tends to be associated with smoking and the use of inhaled steroids (Table 2).

	Frequency	Percentage
Male	40	69 %
Female	18	31 %

Table 2. Male and Female Population Affected with Candidiasis.

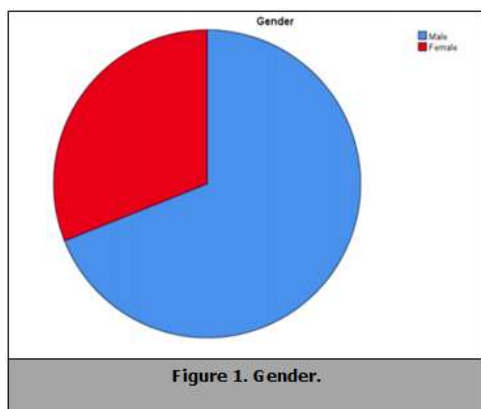
Angular chelates are an erythematous fissure at one or both corners of the mouth, and are usually associated with an intraoral candida infection. Other organisms implicated are *staphylococci* and *streptococci*. In the case of *staphylococci* the reservoir is usually the anterior region of the nostrils and spread to the angles of the mouth has been confirmed by phage typing. Facial wrinkling at the corners of the mouth and along the nasolabial fold especially in older people leads to a chronically moist environment that predisposes to this lesion. This wrinkling is worse in long term denture wearers because there is resorption of bone on which the dentures rest leading to a reduction in height of the lower face when the mouth is closed. Other factors implicated in the aetiology of this condition are iron deficiency anaemia and vitamin B₁₂ deficiency (Table 3).

	Frequency	Percentage
Amphotericin B	1	1.70 %
Clotrimazol	57	98.30 %

Table 3. The Topical Antifungal Therapy was given to the Patient.

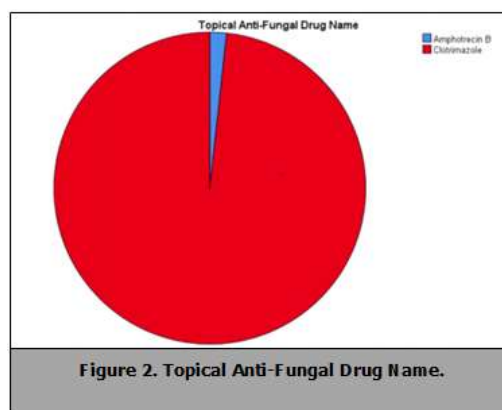
Management

Taking a history followed by a thorough examination of the mouth, looking at the soft and hard palate, and examining the buckle mucosa in those wearing dentures after they have been removed are usually good starting points. Predisposing factors are identified as mentioned above and resolved if possible, and the type, severity, and chronicity of the infection are assessed (Figure 1).¹⁻⁴

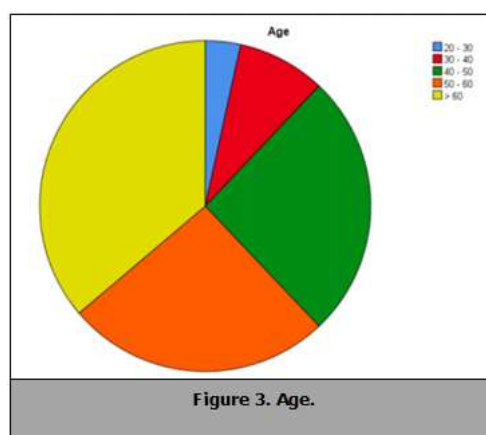


The right diagnosis is usually made on finding the characteristic lesion, ruling out other possibilities, and the response to antifungal treatment. Acute pseudomembranous and chronic atrophic

candidiasis can be treated based on clinical features but culture and sensitivity testing should be undertaken if initial therapy is unsuccessful. Imprint cultures, where sterile foam pads dipped in Sabouraud's broth are placed for 30 seconds on the lesion and then placed on Sabouraud's agar containing chloramphenicol for an hour after which they are incubated, have also been used for identification of *Candida* spp. Acute atrophic and chronic hyperplastic forms may mimic other lesions and a biopsy is recommended in addition to empirical therapy to rule out more serious lesions such as squamous cell carcinoma (Figure 2).



Oral hygiene involves cleaning the teeth, buckle cavity, tongue, and dentures, if present, daily. Dentures should be cleaned and disinfected daily and left out overnight or for at least six hours daily. The dentures should be soaked in a denture cleaning solution such as chlorhexidine as this is more effective in eliminating candida than brushing (Figure 3).



Topical antifungal therapy is the recommended first line treatment for uncomplicated oral candidiasis and where systemic treatment is needed topical therapy should continue as this reduces the dose and duration of systemic treatment required. The systemic adverse effects and drug interactions that

occur with the systemic agents do not occur with topical agents. Treatment in the early part of the 20th century was with gentian violet, an aniline dye, but because of resistance developing and side effects, such as staining of the oral mucosa, it was replaced by a polyene antibiotic, nystatin, discovered in 1951 and amphotericin B, discovered in 1956. They act by binding to sterols in the cell membrane of fungi, and altering cell membrane permeability. Nystatin and amphotericin are not absorbed from the gastrointestinal tract and are used by local application in the mouth. Other drugs belonging to this class are Clotrimazole and Ketoconazole.

Systemic antifungal therapy in oral candidiasis is appropriate in patients intolerant of or refractory to topical treatment and those at high risk of developing systemic infections. Fluconazole is a potent and selective inhibitor of fungal enzymes involved in the synthesis of ergosterol, an important constituent of the plasma cell membrane. It therefore disrupts cell wall formation leading to leakage of cellular contents and cell death. Itraconazole has a wider spectrum of activity than fluconazole and is therefore valuable in salvage treatment of the immunocompromised patients with fluconazole resistant candidiasis.

Prognosis

The prognosis is good for oral candidiasis with appropriate and effective treatment. Relapse when it occurs is more often than not due to poor compliance with therapy, failure to remove and clean dentures appropriately, or inability to resolve the underlying / predisposing factors to the infection.

MATERIALS AND METHODS

A cross sectional retrospective study was done with a population of 58 patients with oral candidiasis visiting Sabetha Dental College and Hospital. The data of the candidiasis was extracted along with the antibiotic prescribed to them most commonly topical. The data was collected from an online patient platform called DIAS, the collected data was tabulated. Data analysis of the collected data was done. SPSS by IBM V26 was used for analysis of the collected data. A Statistical test called Chi-Square test was done.¹⁰⁻¹⁴

RESULTS

From the above data we find that the most males are the most common group of population affected

with candidiasis 40 of them (69 %), female population were 18 people of the collected population (31 %). The collected population was divided into different groups of population according to age group. The first group of population was 20 years to 30 years of age; there were only 2 individuals within that age suffering from oral candidiasis (3.4 %). From the age group of 31 to 40 there were 5 individuals suffering from oral candidiasis (8.6 %). 15 of them from the study were suffering from age group of 41 to 50 years of age (25.9 %). In the age group of 51 to 60 there were individuals suffering from oral candidiasis (25.9 %). 21 of them suffering from oral candidiasis were from the age group above 60 years (36.2 %). The topical antifungal therapy was given to the patient and the most common topical antifungal, given was clotrimazol for 57 patients from the collected sample (98.3 %). Only one patient was given with Amphotericin B (1.7 %).⁵⁻⁹

DISCUSSION

Males are the most commonly affected individuals than females from oral candidiasis. A study conducted by Jolanta E Loster showed that a smaller percentage of the females were not infected by yeast, and the intensity of growth was greater in the female group than among the males, presenting microbiologically as intermediate, intense, and abundant growths of yeast. In our study we found that more than 60 years of age were commonly affected. They also noticed in the study that, in the youngest group of patients (those \leq 50 years of age), the number of uninfected patients was smallest, and was even smaller than the number of subjects with two or more yeast colonies in the oral cavity, it was seen that most of the patients in the study displayed pharyngeal candidiasis. Those in age group 51 - 75 had the highest incidence of candidiasis (39.2 %), whereas those \leq 25 had the least incidence (0.2 %). As well as majority of the patients in the study were between 51 - 75 years of age. In our study amphotericin b was a rare drug used drug in case of topical antifungals of oral candidiasis in a study conducted by Fichtenbaum demonstrated that amphotericin B oral suspension has limited efficacy for the treatment of fluconazole refractory oral candidiasis. In-vitro resistance to amphotericin B is uncommon with Candida species. Amphotericin B oral suspension was approved by the Food and Drug Administration in the 1960 s for the treatment of or pharyngeal candidiasis.¹⁵⁻²² Two small studies have demonstrated by Dewsnup DH and Nguyen MT success with relatively low doses of oral amphotericin B. Some of the important

predisposing factors included xerostomia, antibiotic therapy for prolonged period of time, local chronic trauma or irritation, endocrine disorders, medically compromised states, Fluconazole and clotrimazole are the two commonly used antifungal agents for the treatment of fungal lesions, According to a study conducted by O - Prasertsawat et al. They assessed 103 female patients in a single blinded randomized trial and divided them broadly into two study groups. First group consisted of 53 patients and included participants in whom treatment was done by fluconazole, while the other group consisted of 50 patients and included those in which treatment was done by clotrimazole. They did not observe any significant difference in relation to the clinical characteristic in between the two study groups. They observed approximately 79 % and 80 % mycological cure rates in the two study groups, respectively. They concluded that for the treatment of cases of vulvovaginal candidiasis, fluconazole can be given as an alternative line of treatment. Sekhavat et al. comparatively evaluated the effectiveness of single dose of fluconazole and intravaginal clotrimazole 200 mg per day for 6 days in the patients undergoing treatment for the acute episode of vulvovaginal candidiasis They observed that, at the time of follow-up, during the second visit of the patients, approximately 85 % and 81% of the patients of the group receiving fluconazole were cured clinically and mycological, respectively. Similarly in the other study group, approximately 83 % and 70 % of the study group patients were cured clinically and mycological, respectively.²³

Regarding the pharmacological treatment of candidiasis can be distinguished between two procedures. Topical drugs, which are applied to the affected area and treat superficial infections and systemic drugs that are prescribed when the infection is more widespread and has not been enough with the topical therapy. Systemic treatment, In spite of knowing the efficacy of the drugs listed above, when it comes to a more generalized candidiasis or immunocompromised patients, these would not be sufficient. For those cases would have to resort to treatment with systemic drugs.

CONCLUSION

Males are the most commonly affected individuals with oral candidiasis than females. The most common age group affected was from the age group above 60 years. The most common topical antifungal used for therapy was clotrimazol. It is

found to be more effective in reducing the intensity and lesion of oral candidiasis.

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