Journal of Dentistry and Oral Sciences

ISSN: 2582-3736
Almutairy MF, 2023-J Dent Oral Sci
Review Article

Oral Antifungal Agents for The Treatment of Oral Candidiasis

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Abstract

Candida is considered a fungus which can generally be regarded as a harmless and normal member of the human oral microbiome. The basic principles for management of oral candidiasis are to eliminate and identify underlying host predisposing factors. Yet, in most cases, antifungal agents' therapy will also be needed as a part of the initial treatment. This manuscript provided an overview of clinical management of different types of oral candidiasis with antifungal agents.

Keywords: Treatments; Oral Candidiasis; Antifungal Agents; Oral Medicine; Periodontology

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Receiving Date: 01-09-2023

Accepted Date: 15-09-2023

Published Date: 25-09-2023

Introduction

Oral candidiasis is one of the fungi that frequently infects people with weakened immune systems or altered immunological reactions through Candida albicans. This infection is among the most prevalent fungus infections of the oral mucosa [1].

Candida is regularly found in the mouths of healthy people, and as a result, it is thought that this microorganism represents a typical component of the oral microbiome. According to the particular cohort analysed, the incidence of oral candidal carriage in the general population has historically been estimated to range from 35 percent to 80 percent. The use of molecular testing techniques indicated that Candida species are in fact present in everyone's mouth [2].

Clinical manifestations of oral candidiasis can include pseudomembranous candidiasis, erythematous candidiasis, median rhomboid glossitis, candidal leukoplakia, and angular cheilitis. Most frequently occurs when oral hygiene and denture hygiene are inadequate. Candida albicans creates a biofilm that adheres tenaciously to the base resin of dentures, resulting in denture plaque that has been linked to a number of illnesses [3,4].

Citation: Almutairy MF. Oral Antifungal Agents for The Treatment of Oral Candidiasis. Dent Oral Sci. 2023;5(3): 1-6.
DOI: https://doi.org/10.37191/Mapsci-2582-3736-5(3)-154

This review introduces the antifungal agents that can be used to improve therapeutic profiles. The overall efficacy of these agents has been thoroughly discussed and evaluated.

Aim of the work

To analyze the literature and demonstrate oral antifungal agents for the treatment of oral candidiasis.

Search strategy

A computerized search was conducted for identifying literature on the topic of oral antifungal agents included in the treatment of oral candidiasis. The databases that was accessed include: Sciencedirect, Scopus, Wiley, PubMed, and EbscoHost. The studies that was included were only in English.

Antifungal agents

Contrasted with the broad variety of antibiotics for bacterial infections, there are relatively few antifungal medications on the market, which is likely a reflection of how challenging it is to produce an agent that has effectiveness against eukaryotic cells without the inherent issues of related host toxicity. According to their mode of action and intended target, antifungal medications can be divided into four groups [5]:

- Flucytosine's interference with DNA replication and RNA synthesis.
- Echinocandin antifungals (caspofungin) inhibit the enzymes that synthesise β-1,3 D-glucan.
- The azole family of antifungals, which includes the drugs fluconazole and itraconazole, inhibit the formation of ergosterol.
- Fungal cell membranes disruption, as is the case with amphotericin and nystatin, two polyene antifungals [6].

The first effective antifungal substances developed were polyenes. These medications, which are fungicides, work by interfering with the ergosterol component of the membrane to cause cell membrane porosity, which has the side effect of causing the loss of cytoplasmic content. Although polyenes have a wide range of antifungal action, their usage in dentistry is restricted to topical administration due to their poor intestinal absorption. Amphotericin can be administered intravenously for serious life-threatening forms of systemic candidiasis, although this has a lot of toxicity and adverse effects. Polyenes were the only realistic choice for treating all kinds of oral candidosis prior to the development of azoles [7].

Due to the difficulty in maintaining enough amounts of the antifungal drug in the candida environment, topical polyenes have limited effectiveness in the mouth. This is made even more difficult by polyenes' disagreeable taste, which accelerates salivary flow and lowers the therapeutic amount of the medicine in the saliva. Pharmaceutical companies no longer produce topical amphotericin and all forms of nystatin save for suspension. Although polyenes have been used extensively over the past 60 years, resistance to them by Candida is uncommon, however it can occasionally occur when the ergosterol level of cell membranes decreases [8].

The action of azole antifungals, which are fungistatic, involves interfering with the fungus' lanosterol demethylase enzyme, a necessary step in the manufacture of the ergosterol component of the cell membrane. In ointment or cream form,

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miconazole can also be used in combination with a steroid anti-inflammatory. These miconazole dosage forms can all only be used topically. Other azoles, such as itraconazole, fluconazole, and ketoconazole, on the other hand, are well absorbed by the gut and were the first antifungals that could be given orally for systemic administration. However, severe toxicity is linked to ketoconazole, which limits its therapeutic application [9].

Fluconazole and itraconazole are comparatively safe drugs with few reported side effects. Even when used topically, there is a significant pharmacological interaction between warfarin and azole antifungal medications like miconazole. Concomitant usage of potentized warfarin might cause significant bleeding or even death. Nystatin suspension applied topically may be used by warfarin-taking patients, although as was previously mentioned, its clinical efficacy is subpar [10].

Since dabigatran, a more recent alternative oral anticoagulant medication, does not interact with fluconazole, it may be worth asking the medical professionals who prescribed warfarin if the patient may receive it instead. Warfarin-taking patients who have a substantial oral candidal infection face a challenge because it may not be appropriate or practical to treat them with dabigatran instead of warfarin [6].

A further often observed azole antifungal medication interaction concern is statins. Fluconazole should only be used for the seven days advised to patients, during which time they should be told not to take their statin. Fluconazole is particularly suitable for use in treating oral candidosis since salivary levels of the drug are comparable to those seen in blood. Fluconazole is typically recommended in pill form for out-patients, although it is also available as a suspension if this administration method is necessary. Fluconazole can additionally be injected intravenously. Regrettably, acquired resistance to azole antifungals has developed recently, and some Candida species also naturally resist these medications [11].

There are a number of mechanisms which are found for azole resistance. These mechanisms include, a change in the demethylase enzyme's chemical structures, the evacuation of the azole from the cell by multidrug transporter pumps, and compensation during membrane biosynthesis by other enzymes involved in sterol production. The in vitro susceptibility of a specific Candida strain frequently does not correlate with the following clinical result for patients with oral candidosis, even in the absence of a clearly characterised resistance mechanism. The phenotypic variations between planktonic and biofilm grown cells, the former of which are more usually utilised for in vitro antifungal susceptibility testing, may be one explanation for this [12].

Flucytosine and echinocandin antifungals do not play a role in the outpatient therapy of oral candidosis [13].

Antifungal management of different types

Pseudomembranous candidiasis

The usage of inhaled steroids will be to blame for the great majority of instances of pseudomembranous candidosis seen in primary dental treatment. Fluconazole, 50 mg, given once day for seven days, should be administered as an antifungal treatment. The candidal load will drop to normal levels as a result. The patient should also be told

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that after using an inhaler, they should rinse their mouth with water [14].

Acute erythematous candidiasis

Following the administration of wide spectrum antibiotics, a decrease in the levels of the oral microflora's bacterial component frequently results in the development of acute erythematous candidosis. When antibiotic therapy is stopped, bacteria levels revert to normal, which causes the candidosis to go away on its own. Systemic fluconazole, 50 mg once daily for seven days, may be used if symptoms are severe [15].

Chronic erythematous candidiasis

The elimination of denture colonisation is the main goal of treating this type of candidosis. As a result, miconazole may be inserted in the mouth after being applied topically to the denture's fitting surface. If the denture doesn't have any metal parts, it should be taken out at night and submerged in diluted hypochlorite (typically overnight). To prevent the tarnishing of the metal, dentures containing metal components should not be placed in hypochlorite but rather should be immersed in chlorhexidine [6].

Chronic hyperplastic candidiasis (CHC)

Depending on the severity of the lesions, fluconazole 50 mg daily for a period of seven to forteen days should be prescribed for the treatment of CHC. Additionally, the patient needs to give up smoking. Infection will inevitably return if smoking is not successfully stopped. Patients need to be made aware of the possibility of a malignant change [16].

Secondary forms of oral candidiasis

The aetiology of the oral candidosis should be found and eliminated as part of treatment. The angular cheilitis should go away if treatment is successful. Topical miconazole alone or in conjunction with hydrocortisone should be used to treat the angles' symptoms [6].

Conclusion

A common opportunistic fungal infection that can affect people in the oral cavity is oral candidiasis. Numerous and various forms of antifungal agents can be used for this condition and have recently become the subject of research.

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