

Comparison of oral fluconazole versus itraconazole for treatment of recurrent oral candidiasis

Zaib, Farwa Naqvi*, Saira Mohsin**, Nadeem Yaqoob†, Abdul Mudabbir Rehan††, Ahmad Amin Khan Fraz‡

Department of Dermatology, DHQ Teaching Hospital/ Sargodha Medical College, University of Sargodha, Sargodha.

* Department of Pharmacology, Sargodha Medical College, University of Sargodha, Sargodha.

** Department of Dermatology, Zahida Welfare Hospital Lahore.

† Department of Pharmacology, Niazi Medical and Dental College Sargodha.

†† Department of Pharmacology, D.G. Khan Medical and Dental College, Dera Ghazi Khan.

‡ Physician, Amin Medical Center, Chiniot.

Abstract *Objective* To compare the efficacy of oral fluconazole versus itraconazole in oral candidiasis.

Methods This study was conducted at the Outpatient Department of Dermatology, DHQ Teaching Hospital, Sargodha Medical College Sargodha. A total of 240 patients were included in this study were divided into two groups containing 120 patients in each group. Both groups applied 2% miconazole gel orally thrice daily for 7-14 days. In addition, group A was prescribed fluconazole 50mg once daily and group B was prescribed itraconazole 100mg twice daily for 7-14 days. Each patient was followed up monthly either physically or on phone for 6 months.

Results In group A, the total number of 45 patients (37.5%) reported back with oral candidiasis whereas 19 patients (15.83%) of group B reported back with oral candidiasis.

Conclusion It is concluded that itraconazole is better than fluconazole for the treatment of recurrent oral candidiasis with a similar duration of treatment.

Key words

Fluconazole, itraconazole, recurrent oral candidiasis.

Introduction

Oral candidiasis is a fungal infection of the oral cavity and surrounding area. It is also called oral thrush or oropharyngeal candidiasis or simply candidiasis. Clinically, the patient presents with whitish to yellowish colored plaques commonly on the base of the tongue, sides of the inner cheek, gums, or lips. The patient may complain

of burning or soreness in the affected area and there may be bleeding when the area is scraped. Oral candidiasis is caused by *Candida albicans* which is a common commensal of the oral cavity. It is an opportunistic infection that occurs due to the overgrowth of *Candida albicans* as a result of an imbalance in the innate immunity of the body.

Multiple factors lead to increased infectivity of the pathogen. They include host factors which can be local or systemic. Local factors include reduced saliva production which dilutes the fungus and flushes it out of the mouth. The factors that downgrade the production of saliva

Address for correspondence

Dr. Zaib, Assistant Professor,
Department of Dermatology,
DHQ Teaching Hospital / Sargodha Medical
College, University of Sargodha, Sargodha.
Ph: 03004466409
Email: drzaibahmad@gmail.com

are the destruction of salivary glands by radiotherapy, chemotherapy, Sjögren's syndrome, etc. The use of oral corticosteroids is another contributing factor, as it reduces local immunity.¹ The use of dentures also expedites candidal infection and occurs mostly in elderly immunocompromised patients. Dentures produce an environment that is oxygen-deficient, a good habitat for the growth of fungus.² Other factors that contribute to fungus overgrowth are oral carcinoma, blood dyscrasias, and diet with high carbohydrate content. Iatrogenic factors include broad-spectrum antibiotics which modify the local flora of the oral cavity. Normally the oral flora is restored once the antimicrobial drugs are stopped. Smokers, diabetes mellitus,^{3,4} Cushing's disease can also predispose to oral thrush.

Drug treatment of oral candidiasis is biphasic as we have to treat the underlying cause of the disease as well as the disease itself. First-line treatment of oral candidiasis starts with topical anti-fungal drugs which include nystatin, miconazole, fluconazole, amphotericin B oral suspension. Initially, dermatologists recommend Nystatin oral suspension which is a cheap and readily available choice. Nystatin is poorly absorbed by the gastrointestinal tract so has minimal adverse effects, patients only complain of unpleasant taste. Fluconazole and miconazole oral suspension showed better results than nystatin. When it comes to recurrent oral candidiasis we have to switch to systemic antifungal agents.⁵ Major systemic antifungals are divided into three main groups which include polyenes antifungals (amphotericin B and nystatin), azoles, and echinocandins (anidulafungin, caspofungin, and micafungin). Polyenes antifungal causes pore in the ergosterol cell membrane and increases the permeability of fungus wall leading to fungal death. anorexia, nausea, vomiting, hypersensitivity reactions, drug fever, normocytic normochromic anemia,

cardiac arrhythmias (and even arrest), hepatic dysfunction, CNS signs, and thrombophlebitis at the injection site. Azoles disrupt the synthesis of ergosterol synthesis by inhibiting p450 cytochrome enzyme. They include fluconazole, itraconazole, clotrimazole, miconazole and ketoconazole. Side effects related to azoles include abdominal pain, diarrhea, flatulence, rash, indigestion, etc. Echinocandins noncompetitively inhibit^{1,3} beta-d-glucan synthase enzyme, which is a major component of the fungal cell wall. Normally the adverse effects of echinocandins are mild, but they cause nausea, vomiting, increased bilirubin, and deranged liver function tests.⁶ Systemic antifungals are only employed to treat oral candidiasis when they are unresponsive to topical antifungal treatment.

Methods

This prospective research of the reliable parameters was performed at the Outpatient Department of Dermatology, DHQ Teaching Hospital, Sargodha Medical College, Sargodha. Before commencing the study institutional review board approval was acquired. The patients with recurrent oral candidiasis who voluntarily participated in this study were equally divided into group A and B by using the non-probability sampling technique. The participants were guaranteed full privacy and secrecy during the study. In addition, written informed consent was taken. Total 240 patients aged between 20 and 60 years with history of 4 or more episodes of oral candidiasis within a year were included. All participants who had clinical evidence of oral candidiasis were included in the study. In addition, scraping was taken from the oral cavity, slides were made with KOH and confirmed under the microscope for the presence of *Candida albicans*. Only *Candida albicans* positive patients on a microscope were inducted into this study.

Exclusion criteria include patients with diabetes mellitus,⁴ chronic renal failure (CRF), chronic liver failure (CLD), hyperlipidemia, smoker, drug abuser, or any other connective tissue disorder were excluded. Drug history is very important as patients who took antibiotics, oral contraceptive pills, steroids, hormonal therapy were also excluded from the study. The patient's name, age, gender, address, and mobile number were noted in a pre-designed proforma, so they can be called on the phone for follow-up.

Patients were divided into two groups using a random number table, containing 120 patients in each group. Both groups applied 2% miconazole gel orally thrice daily for 7-14 days. In addition, group A was prescribed fluconazole 50mg once daily and group B was prescribed itraconazole 100mg twice daily for 7-14 days. Each patient was followed up monthly either physically or on phone for 6 months. During the treatment and 6 monthly follow up patient is not allowed to take any multi-vitamin, mouth wash, or medicated toothpaste. A comparison of fluconazole versus itraconazole is shown in tables and figures. The data collected was processed by using Statistical Package for Social Sciences (SPSS 20).

Results

There was a total of 240 patients (both male and female) were selected for this study. Both group A and group B contained 125 patients.

In group A there were 59(49.16%) males and 61(50.83%) females and in group B there were 63(52.5%) males and 57(47.5%) females (**Table 1**).

Table 1 Distribution of patients according to gender.

Gender	Group A	Group B
	n (%age)	n (%age)
Male	59 (49.17%)	63 (52.5%)
Female	61 (50.83%)	57 (47.5%)

Table 2 Distribution of patients according to age.

Age (years)	Patients with recurrent oral candidiasis n (%age)
21-30	21 (9.54%)
31-40	43 (19.55%)
41-50	82 (37.27%)
51-60	74 (33.64%)

Stratification of age is shown in **Table 2** where out of a total of 240 patients with recurrent oral candidiasis majority of patients presented at the age between 41-50 years of age 82 (37.27%). In group A, a total number of 45 patients (37.5%) reported recurrent oral candidiasis. In group B, a total number of 19 patients (15.83%) reported recurrent oral candidiasis.

Table 3 Patients of Group A on fluconazole with recurrent oral candidiasis on follow up (n=120).

Group A Fluconazole	Patients with active oral candidiasis on that follow-up			Patients with recurrent oral candidiasis	
	Total	Male	Female	N	(%age)
1 st follow up	3	3	0	3	2.5
2 nd follow up	8	3	5	11	9.17
3 rd follow up	7	5	2	18	15
4 th follow up	11	6	5	29	24.17
5 th follow up	7	3	4	36	30
6 th follow up	9	5	4	45	37.5

Table 4 Number of patients of Group B on itraconazole with recurrent oral candidiasis on follow up (n=120).

Group B Itraconazole	Patients with active oral candidiasis on that follow-up			patients with recurrent oral candidiasis	
	Total	Male	Female	N	(%age)
1 st follow up	0	0	0	0	0
2 nd follow up	3	0	3	3	2.5
3 rd follow up	5	3	2	8	6.67
4 th follow up	2	1	1	10	8.33
5 th follow up	6	4	2	16	13.33
6 th follow up	3	2	1	19	15.83

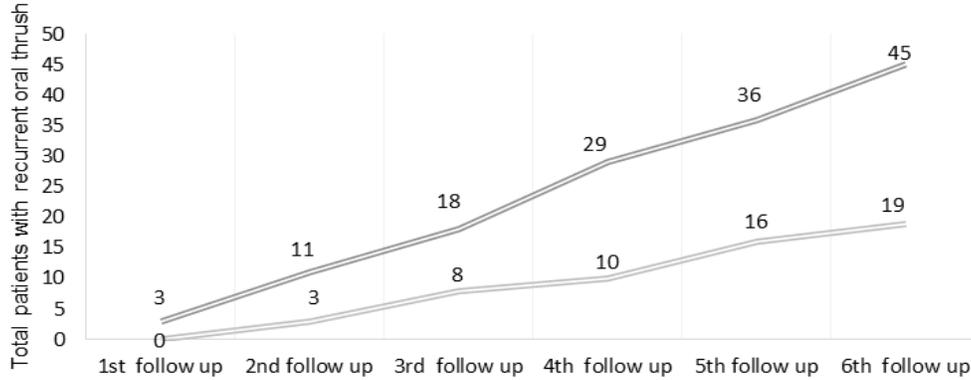


Figure 1 Line chart comparing the number of patients with treatment with fluconazole (group A) versus itraconazole (group B) n=250.

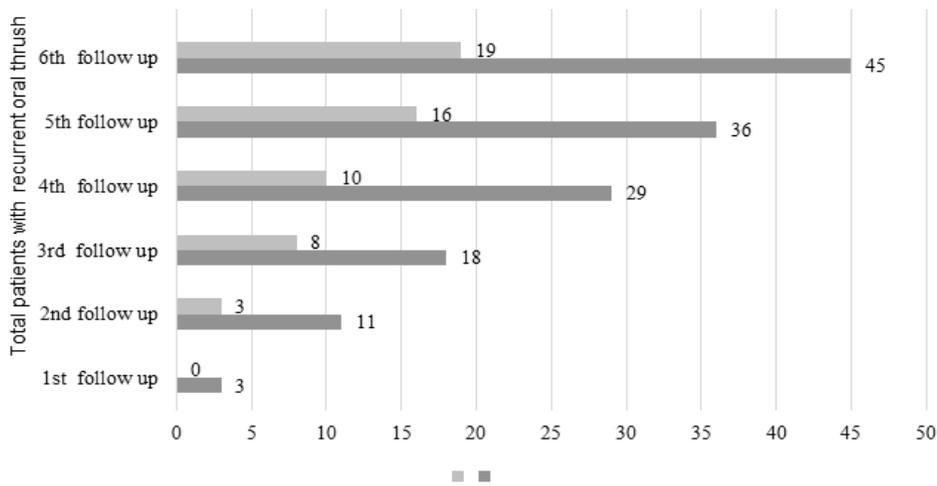


Figure 2 Comparison of the number of patients with treatment with fluconazole (group A) and treatment with itraconazole (group B) n=250.



Figure 3



Figure 4

Discussion

Recurrent resistant oral candidiasis is a common complaint in a medical OPD which is quite a challenge for the patient as well as the physician.

The recurrent oral candidiasis can cause loss of appetite, poor oral hygiene as well as a financial burden on the patient. The causative agent of recurrence should be addressed first. Before starting any drug treatment patients should be

advised to improve oral hygiene. Dentists recommend the removal of dentures at night. Priority should be in treating the predisposing factors and underlying diseases leading to oral candidiasis. It enhances the success of targeted antifungal treatment. Patients are usually treated with topical oral preparations in the beginning. They include topical nystatin⁷ or miconazole preparations. The resistance to topical oral antifungal agents leads to the use of azole antifungals.

Fluconazole is a first-line oral and systemic antifungal agent which is given to patients with recurrent furunculosis. Fluconazole is a very well-investigated antifungal agent for recurrent furunculosis. In a recent study held published in 2017, out of 180 participants were divided into two equal groups which were prescribed fluconazole and clotrimazole. The results showed fluconazole to be a better choice for the treatment of oral candidiasis as fungal eradication was 89.5% by use of fluconazole as compared to 86.7% by clotrimazole.⁸ Itraconazole is another effective systemic antifungal agent. It was given to 32 patients with metastatic breast cancer to treat oral candidiasis, 92.9% of patients were cured.

In our recent study, we compared oral fluconazole and itraconazole for the treatment of recurrent oral candidiasis. We registered a total of 240 volunteers with a history of 4 or more episodes of oral candidiasis. They were divided into two equal groups, group A and group B. Both groups applied 2% miconazole gel orally thrice daily for 7-14 days. In addition, group A participants received tablet fluconazole 50mg once daily and group B received tablet itraconazole 100mg twice daily for 7-14 days. In group A, the total number of 45 patients (37.5%) reported back with oral candidiasis whereas 19 patients (15.83%) of group B reported back with oral candidiasis.

Statistically, on comparison itraconazole was found to be more effective for the treatment of recurrent oral candidiasis than fluconazole.

Conclusion

It is concluded that itraconazole is better than fluconazole for the treatment of recurrent oral candidiasis with a similar duration of treatment.

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