EVALUATION OF CLINICAL EFFICACY OF FLUCONAZOLE MOUTH RINSE FOR TREATMENT OF ORAL CANDIDIASIS

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ABSTRACT

Background: Oral Candidiasis is associated with multiple local and systemic factors. Morbidity and death in high risk patients may be prevented by recognition and adequate management.Flluconazole in a systemic antifungal medication that demonstrate clinical advantage in rinsing before swallowing. The purpose of present study was to evaluate the clinical efficacy of fluconazole aqueous mouth rinses to treat oral candidiasis.**AIM:** To evaluate the clinical efficacy of fluconazole mouth rinse for treatment of oral candiadiasis. **Objectives:** 1) To verify the mycological cure achieved by the drug supported clinical and candida culture.2) To determine the side effects associated with drug**. Material and Methods -** This study group consists of 30 patients who were clinically diagnosed as oral candidiasis and the subjects used 5 ml fluconazole (2mg/ml) mouth rinse 3 times per day rinsing a minimum of 2 minutes and spitting it. The clinical out come and possible adverse effect were assessed after two weeks of treatment.**Results:** Follow –up done for the 30 patients. Complete systematic and clinical relief was noted in 86.66% and mycological cure in 73.3% of the patients. No side effects were reported. **Conclusion:** The use of fluconazole mouth rinses appears to be well tolerated and it is helpful in the treatment of oral Candidiasis effectively.

KEY WORDS: Oral cadidiasis, Fluconazole, candidial culture and anti fungal agent

INTRODUCTION

The oral flora is one of the most ecological diverse microbial populations known to man. It contains at least 350 cultivable species[1],saliva contains up to 100 million organisms per millimetre. Normally the oral flora exists in harmonious relationship with host. The relationship can be altered by any changes to the habitat, which effect stability of micro flora. Changes in the balance between the host micro flora may lead to mucosal infections.[1]

Candida, a fungus, is an obligate associate of human being, thus candida is frequently encountered as harmless commensol of digestive, vaginal tract and constitute a part of normal micro flora of host.

The mere presence of Candida Albicans and other candidal species however does not indicate infection by organism or certainty of subsequent disease. Approximately 60% of healthy adults and 45-65% of health children may harbour commensol candidal organisms without demonstrating any clinical signs or symptoms of mucosal disease.

The fact of an aging population and the use of antibiotics have contributed to the increasing prevalence of oral candidiasis. Oral candidiasis is associated with local factors such as dry mouth, denture and tobacco use and systemic risk factors including immuno-suppressive conditions caused by illness or medications.[2]

Early recognition and prophylactic treatment may prevent serious morbidity and fatal consequences in high risk patients. Antifungal agents are drugs that selectively eliminates fungal pathogens from a host with minimal toxicity to the host. Localized oral candidiasis should be managed initially with local treatment confined to the site of involvement before systemic antifungal drugs are used. Polyene antibiotics have been the initial choice of antifungal for half a century. The azoles have been developed recently and Ketoconazole, Traconazole and Fluconazole are used to treat patients with systemic fungal infection

Fluconazole is one of the newer azoles anti fungal medications has shown to be effective in the treatment of oro-pharyngeal Candidiasis(OPC) and is considered well tolerated and useful medication6 and also demonstrate clinical advantages in topical use as mouth rinse[2.]

The pupose of the present study was to evaluate clinical efficacy of fluconazole mouth rinse for the treatment of oral candidiasis.

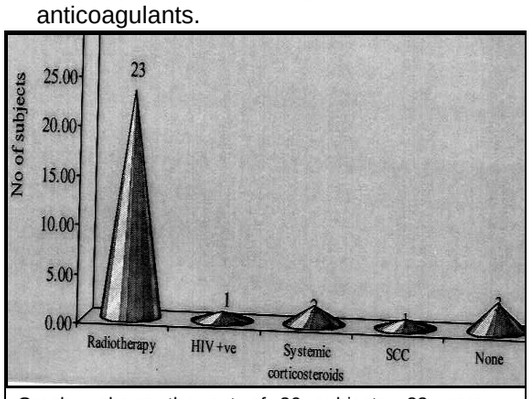
MATERIAL AND METHODS

The study group included 30 patients attending outpatient department of P.N.M.N

dental college and hospital,Bagalkot and Karnataka Cancer therapy and research institute, Hubli who were clinically diagnosed with oral candidiasis. Patients with signs and symptoms of oral candidiasis such as mucosal erythema or adherent white plaques, burning sensation or altered taste were included in the study.(Graph-1). Patients details were recorded in pre formed proforma. A medical history was obtained and all the patients underwent physical examination before initiation of the therapy. Information about medical status was obtained from the hospital records previous episodes of oral candidiasis, and recent use of antifungal therapy the clinical predisposing diagnosis was made.

The following patients are excluded from the study

1) Patients who have used any antifungal agents for a minimum of 2 weeks before the administration of the study drug will be excluded from the study.
2) Chronic alcoholics are excluded.
3) As precautionary pregnant women are excluded.
4) If patients known sensitivity to triazole derivatives are excluded in the study.
5) If they were taking barbiturates or anticoagulants.



Graph shows the out of 30 subjects, 23 were undergoing radiotherapy, 2 were undergoing systemic corticosteroid therapy, 1 HIV positive, 1 SCC and remaining 3 subjects were not associated with medical history.

Graph-1. Distribution of Study subjects according to the Medical status.

Visual analogue scale was used for evaluation of burning sensation. The patient is asked to grade oral discomfort as mile, moderate and severe.

0 - No burning sensation
1. Mild burning sensation
2. Moderate sensation
3. Severe sensation

The clinical signs were categorized in to mild, moderate, severe based on the extent of the lesion in the oral cavity. They are categorized under scores

Score 1 - Mild if it involves one or two localized areas
Score 2 - Moderate it involves more than two localized areas
Score 3 - Severe if there is generalized involvement.

Sampling Method for Candidal Culture

This study was conducted in the department of oral medicine and radiology P.M.N.M Dental College and hospital, Bagalkot, source of subjects for the study was from research institute, Hubli. A total of 30 patients were included. The patients in our study commonly presented of all age groups with a clinical and microbiological diagnosis of oral candidiasis included in the study.

The method of sampling from oral cavity for the isolation of Candida in our study is concentrated oral rinse. The patients asked to rinse the mouth 60s with 10 ml of sterile phosphate buffered saline (PBS) and patient then returns the oral rinse to the universal container. Sample is transported immediately to the laboratory where they were cultured with the use of standard techniques.

Patients (n=30) given a suspension of 2mg/ml of fluconazole in distilled water (with no sweeteners and flavouring agents) which, was prepared by a pharmacist in prescription form, (HSK College of pharmacy, Bagalkot) stored in amber coloured bottles and kept refrigerated during clinical use. Each patient was instructed to rinse with 5ml (2mg/ml) is equal to 10mg of fluconazole mouth rinse solution for 2 minutes, 3 times a day and then spitting it out. Patients were also instructed to avoid water or food for 2 hours after rinsing for a period of 2 weeks, patients were recalled after 2 weeks, examined for clinical signs and symptoms, once again mycological assessment was done by using concentrated oral rinse technique as performed before treatment. Patients adverse effects associated with the fluconazole mouth rinse were noted.

Mycological assessment

Candida colony counts were obtained

using sabourauds dextrose agar Inoculation, incubation and colony collection

Each specimen was inoculated on sabourauds dextrose agar. The plates were incubated aerobically 37 C for 24 - 48 hours the plates were examined. The yeast colonies of the saliva samples were counted and calculated as the number of colony forming units per millilitres (cfu m -1) of rinse.

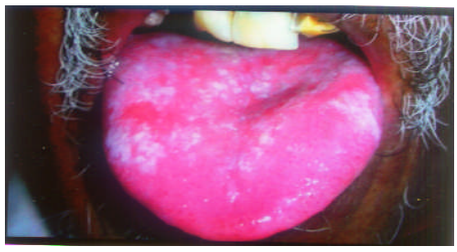
Results

Data was entered in to the computer and frequency tables were generated using SPSS software version 11.00. WILCOXAN'S matched pair tests were used for comparison of clinical sign and mycological cure before and after treatment. The statistical significance set at 5% level of significance ($p<0.05$).

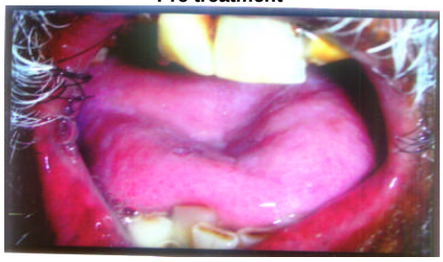
Discussion

The increased use of antibiotics and immunosuppressive agents and advances in medical management including chemotherapy, immunosuppressive therapy, and invasive surgical procedures, contribute to the increased in candidal infection.[3]

In addition, the severity of candidiasis of the oropharynx, commonly associated with HIV infection, may be predictive of the progression of the disease acquired immunodeficiency syndrome in those patients[4].



Pre treatment

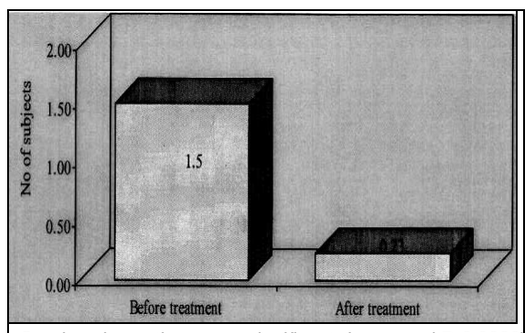


Post treatment

Fig 1. Clinical resolution of the lesion

Candida is common, harmless dimorphic yeast that lives without producing disease in the oral cavities of up to 40% normal individuals. But are present in the mouth of healthy carrier in a low concentration of 200-500 cells per millimetre of saliva[5]at this concentration the organism cannot be usually identified by direct microscopic examination of smears from the oral mucosa and its presence can be demonstrated only by inoculation on a selective medium such as subourauds agar.

Topical therapy is generally effective in controlling low grade uncomplicated mucosal candidiasis. In cases of severe oral candidiasis, topical therapy in conjunction with systemic therapy may ensure a lower systemic dose and shorten the duration of the high dose systemic antifungal therapy. In our study, 30 patients were enrolled and were given Fluconazole mouth rinse in the dose of 2mg/ml where the patients were advised to swish 5ml of the solution for 2minutes and spitting it out. This was performs trice daily according for a total daily dose of 30mg/ day.



Graph shows there was significant decrease (P 0.0000) in clinical signs after treatment (0.23) when compared to before treatment (1.50).

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Graph-2. Comparison of mean clinical signs before and after treatment.

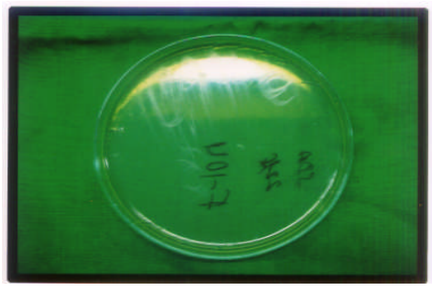
In our study, the clinical resolution rate of fluconazole mouth rinse {(Fig.1) (Graph-2)} were found to be 86.66% and mycological cure about 73.33%, where as study conducted by Koletar SL (1990)[6] in the preliminary investigation of 39 adult patients with HIV infection and oral candidiasis, reported a clinical resolution rate of 100% for Fluconazole group. However the drug dosage used in his study was much higher (Fluconazole capsule – 100mg daily for 2 weeks) and secondly the drug was given by systemic route.

In a study conducted by Flynn P.M. (1995)[7] et al the clinical cure was demonstrated 91% and mycological cure of 76% where the patients received fluconazole suspension systemically, where in our study clinical cure was

86.66% and mycological cure 73.33% rate comparatively higher rate of clinical cure in their study was due to contact of oral suspension with oral mucosa before being ingested, which offer added advantage along with systemic treatment. In their study 6 patients in the fluconazole group developed gastrointestinal upset as adverse effect. In our study none of the patient experienced any effect from the treatment.

In our study, mycological cure was 73.33% with topical mouth rinse (Fig.2) where as study conducted by Pons V et al (1997) [8] were with fluconazole oral suspension showed mycological cure of 60%. This shows that mouth rinse is better than oral suspension.

Growth Of Candida Before Treatment showing plenty of colonies on SDA culture plate



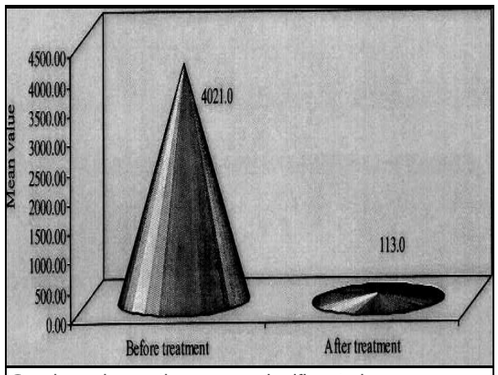
Growth Of Candida After Treatment showing NO colonies on SDA culture plate

Fig. 2. Mycological cure rate

In a study conducted by Joel B. Epstein (2002)[2] similar treatment protocol as in our study was used and showed no adverse effects. Our study is being consistent with above study.

In our study, l HIV Sero positive individual with CD4 count 50 cells per millimetre showed no clinical and mycological cure. This was consistent with the study conducted by P Diz Dios (1995)[9]. Out of 30 patients in their study 4 patients showed no clinical and mycological cure. The reason being impaired immune status with CD4 lymphocyte counts less than 50 cells per mm3, and secondly there were no cure to poor patient compliance.

In our study, pseudo membranous candidiasis accounted for 86.67% erythamatous candidiasis 3.33% , denture stomatitis 6.67% of cases, median rhomboid glossitis 3.33%. The classic form of candidiasis is the pseudo membranous form followed by denture stomatitis, acute erythamatous candidiasis. This finding was consistent with the finding with other studies[2].



Graph shows there was significant decrease P0.0000) in candidial colony counts after treatmen (113.00) when compared to before treatment (4021.00) .

Graph-2. Comparison of mean colony counts before and after treatment.

The advantages of mouth rinse over type of applications are as follows. First, in patients with dry mouth, tablets given to dissolve in the mouth may be poorly soluble. Joel B. Epstein (2002)[2] reported the fluconazole is detected in saliva 2 hours after systemic administration. On the other hand, Fluconazole mouth rinse enhances the drug exposure of the oral mucosa immediately, and lasts for 4 hours, compared with the same dose administered by systemic route. Because the pathogenic micro organism in oral candidiasis are usually in the superficial layers of the oral mucosa, the effectiveness of this mouth rinse may be attributed to the temporary higher concentration at required site, resulting in improved efficacy. Secondly this mouth rinse lacks the risk of systemic adverse effects and drug interactions.

None of our patient noticed adverse effects. However in literature Gussenhover MS et al (1991)[10], reported a case of Stevens-Johnson syndrome, which occurred as a result of adverse effect to fluconazole. C. Wells AML Lever also reported liver toxicity in a HIV patient, which on

biopsy showed a central lobular cholestasis, which was consistent with fluconazole toxicity.[11]

However mouth rinse may not be effective in wide spread severe oral candidiasis in immune compromised patients. This could be one of its disadvantages when compared to systemic drug therapy. However, one disadvantage of mouth rinses that, it may not effective at the corner of mouth (in case of angular cheilitis) when used.

There were certain limitations in our study. Patients were not followed up after 2 weeks foe any possibility of recurrence. Patients were only asked about side effects but were not assessed objectively for any liver damage. However, although the number of patients in the present study was small, the outcome was promising, more so because the dose of Fluconazole used per day was only 30mg, which is less than 1/3rd of the standard dose of Fluconazole.

CONCLUSION

The Treatment With Floconazole Is Well Tolerated. The Results Of This Study Can Be Used As Basis For Further Studies With Large Sample Of Patients With Oral Candidiasis To Check Clinical Efficacy Of Fluconazole Aqueous Mouth Rinse. The Dentists Should Employ A More Conservative Intervention With Oral Mouth Rinses For Mild To Moderate Cases Rather Than Risk Adverse Effects And Complication Of Systemic Drugs For The Management Of Oral Candidiasis.

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