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AZOLES ON RECALCITRANT CUTANEOUS DERMATOPHYTOSIS IN A TERITARY CARE HOSPITAL

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ABSTRACT

Background: There is an increasing number of recalcitrant dermatophytosis cases in recent years. The standard treatment dosimetry is no longer effective in achieving clearance and results in high failure rate whereas combination therapy is a well-established concept in the treatment of recalcitrant dermatophytosis. **Objective:** To evaluate the efficacy and safety of oral Itraconazole and pulse fluconazole combination therapy along with topical ciclopirox olamine in the management of dermatophytosis. **Methods:** 200 Clinically diagnosed and KOH positive patients of tinea corporis/cruris were taken into our study and given itraconazole 200mg for 3 weeks and fluconazole 150mg pulse twice a week for 6 weeks along with topical antifungal once daily for 6 weeks. Patients were followed up at 3, 6, and 9 weeks. Adverse effects were noted at the end of therapy. **Results:** Cure rate of 90% is noted after 3 weeks of treatment, 93% at the end of 4th week of treatment and a maximum cure rate of 95% was achieved by 6th week, however recurrence of 2 patients was observed at 9th week follow up. Adverse affects were mild and patients were adherent with the study. **Conclusions:** The combination of systemic Itraconazole and fluconazole therapy may be an effective and safe therapeutic strategy and comparatively more effective than monotherapy in the management of dermatophytosis

KEYWORDS: Dermatophytosis • Itraconazole • Fluconazole • Ciclopirox olamine.

INTRODUCTION

Dermatophytes are pathogenic fungi that have the capacity to invade keratinized structures such as skin, hair, and nails causing dermatophytosis which are caused by Trichophyton, Microsporum, and Epidermophyton They are a worldwide public health problem affecting more than 20–25% of the world's population, with varying geographic distribution,[1] It is more prevalent in developing, particularly in tropical and subtropical countries like India, evidently due to the hot and humid climatic conditions.[2]

Dermatophytosis are treated with combination therapy with topical along with systemic antifungal drugs. At present, topical antifungal agents like clotrimazole, naftifine, ciclopirox olamine, and systemic antifungal agents like itraconazole, fluconazole and terbinafine have been introduced into clinical practice during last 5-10 years for effectively treating dermatophytosis.[3] The levels of various oral antifungals in the skin depend on the route of delivery of antifungals and can be via sebum, sweat, keratin, or via diffusion through the dermis.[4] Though the approved dose of itraconazole remains 100-200 mg for a duration of 2 to 4 weeks, depending on the site of the infection, there are increasing instances of patients not responding adequately to this dosimetry. Thus, in situations where either the site of infection has less sebum or the patient has an intrinsically dry skin or in case of clinical failures without resistance, fluconazole may be the ideal drug, as it has the highest levels in the stratum corneum.[5] The combination therapy is a well-established concept of using synergistic and additive effects of two or more drugs to improve therapeutic efficacy and overcome drug resistance.

The aim of this study was to combine the advantages of azoles and use in recalcitrant cutaneous dermatophytosis and follow up the cases and to provide a low cost effective treatment.

MATERIALS AND METHODS

This study was carried out in Navodaya medical college hospital and research centre in Karnataka. A case series evaluation was undertaken of 200 KOH positive and clinically diagnosed patients between the age group of 18 -55 years for a duration 6 months who presented with lesions suggestive of Tinea corporis/cruris/both.

The skin scrapings were subjected to culture on Sabouraud dextrose agar (SDA). A detailed clinical history including duration of infection, family history,

triggering factors, treatment history, occupation and systemic symptoms.

Patients with recalcitrant cutaneous dermatophytosis with history of treatment with azoles are taken into our study. Patients with known Cardiac disorders, Renal disorders, HTN, Immunosupression /Immunosupressive drug intake, Tinea capitis, Tinea pedis, age >55years, women in pregnancy and lactation are excluded from our study.

Investigations such as KOH mount, Fungal culture and sensitivity and LFTs are done before and after the study.

The patients are consecutively provided with Itraconazole 100mg twice a day before food for 3 weeks along with pulse Fluconazole 150 mg twice a week for 6 weeks along with topical ciclopirox olamine for 6 weeks in no particular brand. Further, patients were followed up at the end of 3,6 and 9 weeks to look for resolution and recurrence (i.e new lesions of tinea in patients who initially showed complete clearance of lesions at 3 week). The patients were asked about any side effects experienced during the treatment course.

RESULTS

In our study, Tinea cruris with concurrent tinea corporis was the most frequent clinical presentation. KOH showed fungal hyphae in 100% Culture was positive in 88 % patients. Trichophyton mentagrophytes was the most common isolate (46.6%) followed by Trichophyton rubrum (28.3%). Among 200 patient, 67% (134) were males and 33% (66) were females. Major age group in our study were between 40-55 years of age 39% (78) followed by 18-30 years 34% (68) and 27% patients were in age group of 30-40 years. At 3 weeks follow up, 90% (180) of the patients had improvement which was statistically significant. Clinical as well as mycological cure rate was seen by 4 weeks which is 93% (186) of patients. Follow up at 6 weeks showed maximum number cure rate in 95% (190) of cases. At 9 weeks, 2 patient showed recurrence.

Adverse effects were noted in 8 (4%) patients such as headache, nausea and insomnia. Mild rise in liver transaminases were noted in one patient. However, the enzymes levels returned to normal limits at subsequent follow up.

Table 1: Fungal culture results.

Culture positive	88%
Trichophyton mentagrophytes	46.6%
Trichophyton rubrum	28.3%

Table 2: Sex wise distribution.

Total no of patients	200	100%
Males	134	67%
females	66	33%

Table 3: Age wise distribution.

Total no of patients	200	100%
18-30	68	34%
30-40	54	27%
40-55	78	39%

Table 4: Cure rate.

Duration	Cure rate
3 weeks	90%
6 weeks	93%
9 weeks	95%

DISCUSSION

The levels of various oral antifungals in the skin depend on the route of delivery of antifungals and can be via sebum, sweat, keratin, or via diffusion through the dermis.[4]

The approved dose of itraconazole is 100-200 mg for a duration of 2 to 4 weeks, depending on the site of the infection, there are increasing studies which depict the raising number of recalcitrant cases with this dorsimetry. Thus, in situations where either the site of infection has less sebum or the patient has an intrinsically dry skin or in case of clinical failures without resistance, fluconazole (FLU) may be the ideal drug, as it has the highest levels in the stratum corneum. It is suggested that a high concentration of an antifungal agent is required in the stratum corneum and epidermis–dermis junction for efficacy against dermatophytosis.[6]

The second-generation azoles, Itraconazole and Fluconazole act on ergosterol biosynthesis at the C-14 demethylation stage, a three step, oxidative reaction catalysed by the cytochrome P-450 enzyme – 14α-lanosterol demethylase (P-450DM).[10] Severe ergosterol inhibition (>99%) additionally interferes with the sparking functions, affecting cell growth and proliferation.[11]

Fluconazole has good oral bioavailability, accumulates rapidly in Stratum corneum and achieves high levels. FLU was initially used in a dose of 50 mg/day but later in view of the skin Pharmacokinetics characteristics, a weekly dose of 150 mg was tried in trials and reported to be effective.[12]

In the present study, 3 weeks treatment with itraconazole 200 mg/day along with pulse fluconazole 150mg twice a week showed cure rate of 90% which was similar a study done by Sharma et al, where Itraconazole 200mg once a day along with pulsed intermittent therapy of terbinafine 250mg three times weekly showed cure rate of 91.3%.[13] Studies using Itraconazole along with Pulse fluconazole therapy have not been as of our knowledge.

Combination therapy of itraconazole and pulse fluconazole was found to have a significantly higher clinical and mycological cure rate of 90% at 3 weeks as compared to monotherapy with the same drugs. The

combination therapy was found to have the lowest recurrence rate when compared to monotherapy with either of the drugs.

All the adverse effects were of mild in severity and none of the patients required discontinuation of therapy. Adherence to treatment was excellent in our study. In this study, the combination of fluconazole and itraconazole was found to be as safe as monotherapy. This combination can thus limit the duration of treatment, is well tolerated and does not appear to have significant adverse effects. New vistas of antifungal combination therapy appear to have promising future in the prompt management of treatment failures of dermatophytosis.

CONCLUSIONS

The combination of systemic Itraconazole and fluconazole therapy may be an effective and safe therapeutic strategy and comparatively more effective than monotherapy in the management of dermatophytosis.

REFERENCES

1. Havlickova B, Czaika VA, Friedrich M. Epidemiological trends in skin mycoses worldwide. Mycoses, 2008; 51(4): 2–15.
2. Verma S, Madhu R. The great Indian epidemic of superficial dermatophytosis: An appraisal. Indian J Dermatol, 2017; 62(3): 227-36.
3. Maurya VK, Kachhwaha D, Bora A, Khatri PK, Rathore L. Determination of antifungal minimum inhibitory concentration and its clinical correlation among treatment failure cases of dermatophytosis. J Family Med Prim Care, 2019; 8(8): 2577-81.
4. Andes D. Pharmacokinetics and pharmacodynamics of antifungals. Infect Dis Clin North Am, 2006; 20(3): 679-97.
5. Sardana K, Arora P, Mahajan K. Intracutaneous pharmacokinetics of oral antifungals and their relevance in recalcitrant cutaneous dermatophytosis: Time to revisit basics. Indian J Dermatol Venereol Leprol, 2017; 83(6): 730-2.
6. Faergemann J, Laufen H. Levels of fluconazole in serum, stratum corneum, epidermis-dermis (without stratum corneum) and eccrine sweat. Clin Exp Dermatol, 1993; 18(2): 102-6.
7. Katsambas A, Antoniou C, Frangouli E, et al. Itraconazole in the treatment of tinea corporis and tinea cruris. Clin Exp Dermatol, 1993; 18(4): 322–35.
8. Noppakun N, Phuphaibool K. Treatment of dermatophytosis with new systemic antifungal agent, itraconazole. J Med Assoc Thai, 1992; 75(2): 99–103.
9. Bourlond A, Lachapelle JM, Aussems J, et al. Double-blind comparison of itraconazole with griseofulvin in the treatment of tinea corporis and tinea cruris. Int J Dermatol, 1989; 28(6): 410–2.
10. VandenBossche H, Marichal P, Le Jeune L, et al. Effects of itraconazole on cytochrome P-450-dependent sterol 14a-demethylation and reduction of 3-ketosteroids in Cryptococcus neoforinans. Antimicrob. Agents Chemother, 1993; 37(10): 2101–5.
11. Barrett-Bee K, Newboult L, Pinder P. Biochemical changes associated with the antifungal action of the triazole ICI 153,066 on Candida albicans and Trichophyton quinckeanum. FEMS Microbiol. Lett., 1991; 63(2-3): 127–32.
12. Stary A, Sarnow E. Fluconazole in the treatment of tinea corporis and tinea cruris. Dermatology, 1998; 196(2): 237–41.
13. Sharma P, Bhalla M, Gurvinder P T, Chander J. Evaluation of efficacy and safety of oral terbinafine and itraconazole combination therapy in the management of dermatophytosis, Journal of Dermatological Treatment, 2020; 31(7): 749-53.