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Original Research Article

Comparative Assessment of Oral Terbinafine versus Itraconazole in Tinea Corporis and Cruris

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Abstract

The management of dermatophytosis is challenging in India and there are reports of using systemic antifungals at higher doses. But there are multiple reports of increased treatment failures with terbinafine at standard dosage as well. To assess this a randomized, open label, comparative study was conducted where 80 patients with tinea corporis et cruris infection were included. Patients were either prescribed terbinafine 250mg twice a day or itraconazole 100mg twice a day for 4 weeks. Efficacy was assessed based on complete, clinical and mycological cure rate. At the end of six weeks, there was a statistically significant improvement (p value<0.05) in the total symptom score (erythema, scaling, and pruritus) in Group I as well as in Group II compared to baseline. None of the patients showed any significant side effect in both Itraconazole and Terbinafine groups. No changes in liver function were observed in both the groups. This study shows that the high dose of terbinafine in combination with topical ciclopirox is effective and safe in management of tinea corporis et cruris.

Keywords: T corporis, dermatophytosis, terbinafine, Itraconazole

Introduction

Dermatophytosis is among the most common fungal infection affecting 20%–25% population globally, with varying geographic distribution. [1,2] Due to our countries hot and humid climate, there has been a rampant elevation in the cases of dermatophytosis and atypical presentation in recent times. [3,4] Additionally, the recommended treatment of commonly prescribed anti-fungal agents no longer seems to be valid in the current scenario, resulting in treatment failures and relapses when given in conventional doses and for standard duration. [5] Hence, the management of dermatophytosis is becoming more subjective in order to overcome these challenges. [6,7] Moreover, the choice of therapy is further influenced by multiple factors like simultaneous involvement of extensive body area, hair follicles and a previous history of treatment failures, recurrences and relapses. 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. [8]

Studies have reported that while using combination therapy, drugs from two different classes should be used for wider

coverage, synergistic or additive action and to reduce the chance of resistance. For the management of dermatophytosis, Terbinafine is considered to be a first-line drug due to its favourable mycological and pharmacokinetic profile. [9]

Till recent years, the drug was consistently effective with cure rates of >90% achieved at doses of 250 mg once a day for two weeks. [9,10] But recently, due to the overuse of the drug, there has been an increase in the incidence of terbinafine resistance resulting in increasing numbers of clinical failures and relapses. [11,12] Hence it is advisable to use higher dose of terbinafine

Itraconazole is another antifungal drug which acts by inhibiting ergosterol synthesis. It has shown good results in the treatment of dermatophytosis at doses of 100 mg once a day for two weeks and with 200 mg once a day for seven days. [13,14] But due to frequent relapses at short intervals, some physicians in India have used it in doses of 200 mg once a day for prolonged periods. [7,15]

Recently, a combination of itraconazole and terbinafine has also been studied 22 suggesting need of either high dose or combined dose of different systemic antifungals in current settings in India. But there is no studies comparing high dose of terbinafine against standard dose of itraconazole. Hence, the present study was conducted to compare the effectiveness and safety of combination of high dose of oral terbinafine and CPO versus standard dose of itraconazole and CPO in the management of dermatophytic infections among the selected popupation in southern rajasthan.

Methodology

we conducted a prospective, observational study in the dermatology outpatient of a tertiary care hospital in Udaipur Rajasthan. Clinically confirmed cases of tinea corporis et cruris were recruited for the study and followed up for 8 weeks, till the completion of their treatment. All consenting patients, in the age group of 18-65 years, who were diagnosed by the specialist as suffering from tinea corporis et cruris were included in the study, irrespective of the presence and extent of dermatophytosis in other regions of the body. Patients who were pregnant, lactating, non-consensual, as well as those who had a history of anti-mycotic treatment within 2 weeks prior to baseline visit were excluded from the study. The patients were randomly allocated either to Itraconazole 100 mg twice a day (Group I) or Terbinafine 250 mg twice a day (Group II) for four weeks. Both the groups received additional topical Ciclopirox Olamine cream for six weeks along with antihistamines.

The study was approved by the Institutional Ethics Committee, and informed consent was taken from all patients before recruiting. KOH examination was done at the time of enrolling the patient and at the end of the sixth week. Fungal culture was done in all KOH positive patients only at the beginning of the therapy. Liver function tests were done at the start of the therapy and at the end of the fourth week. At each visit, a clinical assessment was made. The therapeutic efficacy was evaluated at six weeks. Patients were considered cured when there was an absence of any signs and symptoms and negative KOH.

Observations

A total of 80 patients were randomly assigned treatment and included in the study. The two groups had 40 patients each. The average age of the patients was 38.28 and 33.25 years, respectively, in Group I and Group II. There were 20 males and 20 females in Group I, while Group II had 17 males and 23 females. All the patients were co- prescribed CPO and antihistamines.

At the end of six weeks, there was a statistically significant improvement (p value<0.05) in the total symptom score (erythema, scaling, and pruritus) in Group I

as well as in Group II compared to baseline [Figure 1]. The significant improvement started from 0-2 weeks and then persisted till the end of the treatment in both the groups. On comparing the groups, there was a significant improvement in the total symptom score at the end of four weeks (p value<0.05) but no statistically significant change was observed at the end of 6 weeks (p value>0.05).

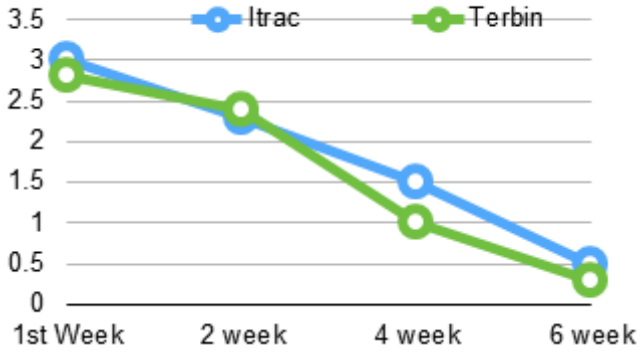

Figure 1: Symptom Progression

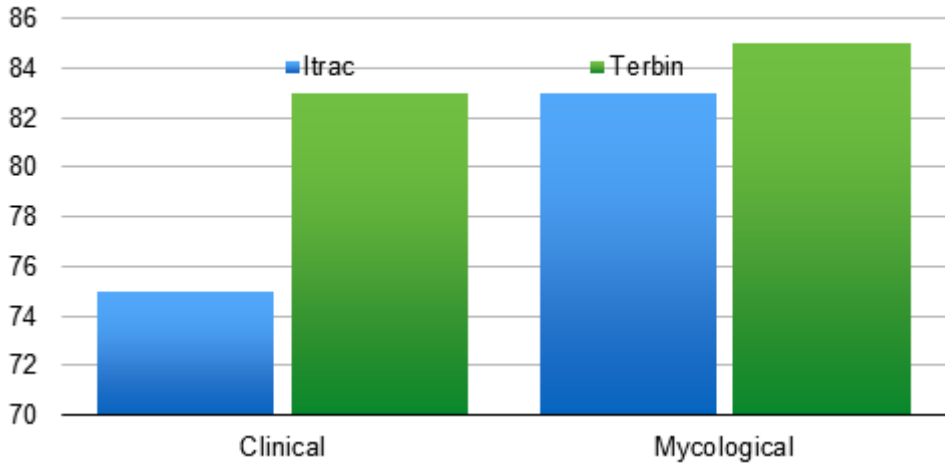

Figure 2: Cure Rates

Mycological cure was achieved in 32 patients (80%) in Group I and 34 patients (85%) in Group II at the end of six weeks, whereas complete cure was achieved in 29 patients (72.50%) and 31 patients (77.5%) in Group I and II respectively at the end of six weeks. Twenty five percent of the patients achieved clinical cure at the end of four weeks in Group II which increased to 85% at the end of six weeks (Figure 2).

None of the patients showed any significant side effect in both Itraconazole and Terbinafine groups. No significant change in LFTs was also observed in both the groups during the study period.

Discussion:

Based on initial studies and recommendations, topical antifungals are the first line drugs in the management of dermatophytosis. However, in the current clinical scenario in India, patients with large lesions or multisite dermatophytosis, only topical therapy fails to clear the lesions, leading to treatment failures and relapses. In such patients, systemic therapy is often recommended. Recently, Sahoo et al. [16] and Murlidhar et al. [17] in their comprehensive reviews recommended the use of a combination of topical and systemic antifungals in the management of

patients with large lesions or recalcitrant tinea infections.

Though combination therapy is widely practised in India, not much of the literature is available regarding the effectiveness of the combination therapy. Only two study is available indicating efficacy of combination therapy. [18,19] As per this study, terbinafine with sertaconazole achieved better efficacy than itraconazole and sertaconazole combination though results are not statistically significant. Secondly, there is still the question on the right combination of systemic and topical anti-fungal agents.

In our study, both the combination therapy options were efficacious in the management of dermatophytosis. Although the patients in Group II achieved clinical cure much faster as compared to Group I, there is no statistical difference in the complete cure at the end of six weeks.

A recent study by Majid et al. [12] could achieve only 43% cure rate after two weeks of daily 250mg terbinafine oral treatment in dermatophytosis. This recent decrease in the clinical efficacy is well corroborated by an upsurge in the cases encountered by dermatologists in daily clinical practice along with a failure to respond to the standard oral terbinafine therapy. Another study showed the mycological cure rate of terbinafine as 74% 20 and 71%. In all these studies, terbinafine 250 mg/day was used. But in our study, we have used terbinafine in the dose of 500 mg/day, which was well supported by some recent studies.

In a recent study, three-week treatment with itraconazole 200 mg/day showed a cure rate of 50% which was lower as compared to previous studies showing variable cure rates of 80-92%. [16,20] These variable results of clinical efficacy of itraconazole are well evidenced in some of the literature. In our study, the mycological cure rates in Group I and II were 82% and 84% respectively. [21] Though the mycological cure rate is similar to recently done studies in the itraconazole group, in the terbinafine group, it is better than previous studies. This clearly indicates the need of using a higher dose of terbinafine along with a topical anti-fungal agent. [22]

Conclusion

In the standard dosage, terbinafine and itraconazole have been used extensively for the treatment of dermatophytosis and have been found to be safe and well tolerated. 6,21 In the present study, the duration of the combination therapy was only four weeks, but all the patients continued with topical for another two weeks. At the end of four weeks, patients in the terbinafine group showed good clinical resolution but in the itraconazole group, there was partial clinical response. But at the end of six weeks, patients in both the groups showed marked improvement indicating beneficial extended use of topical therapy. This indicates the need of monotherapy with topical for an extended duration in order to achieve higher cure rates in the treatment of dermatophytosis

Limitations of our study include its small sample size and short duration of follow-ups. Due to short duration of the follow-ups, we could not evaluate patients' relapse rates. Additionally, this study was conducted at a single centre and hence these findings cannot be generalized. For this purpose, further multicentre studies with larger sample size are required.

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