Int. j. adv. multidisc. res. stud. 2024; 4(3):470-475

Received: 01-04-2024
Accepted: 10-05-2024

International Journal of Advanced Multidisciplinary Research and Studies

ISSN: 2583-049X

Comparison on Efficacy between Itraconazole and Terbinafine in the Treatment of Cutaneous Dermatophytosis

[1] Farhana Yeasmin, [2] Shahin Ara, [3] Lubna Khondker, [4] Md. Nazrul Islam, [5] Ibrahim Md. Sharaf, [6] Nelofar Yasmin, [7] Gulam Kazem Ali Ahmad

[1] Lecturer, Department of Pharmacology & Therapeutics, Rajshahi Medical College, Rajshahi, Bangladesh
[2] Head, Department of Pharmacology & Therapeutics, Rajshahi Medical College, Rajshahi, Bangladesh
[3] Associate Professor, Department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh
[4] Assistant Professor, Department of Dermatology and Venereology, Rajshahi Medical College Hospital, Rajshahi, Bangladesh
[5] Medical Officer, Department of Dermatology and Venereology, Rajshahi Medical College Hospital, Rajshahi, Bangladesh
[6] Lecturer, Department of Community Medicine, Rajshahi Medical College, Rajshahi, Bangladesh
[7] Consultant, Popular Diagnostic Centre Ltd, Rajshahi, Bangladesh

DOI: https://doi.org/10.62225/2583049X.2024.4.3.2810
Corresponding Author: **Lubna Khondker**

Abstract

The increasing burden of dermatophytosis has been observed all over the world. The vast numbers of hidden and undiagnosed cases remain untreated and these patients act as reservoirs and reinfect their surroundings, contributing to communal infection, a significant threat to the community. This randomized clinical trial was conducted to compare efficacy & safety between Itraconazole and Terbinafine in the treatment of cutaneous dermatophytosis, in the Department of Pharmacology and Therapeutics at Rajshahi Medical College, Rajshahi in collaboration with department of Dermatology & Venereology at Rajshahi Medical College Hospital, Rajshahi and Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh from July 2021 to June 2022. The study was conducted after obtaining ethical clearance from the Institutional Review Board (IRB) of Rajshahi Medical College and consent from the patients. Based on predefined eligibility criteria, a total number of 180 patients with dermatophytosis were included in the study. The study population was divided into two groups (Group-A and Group-B) on the basis of drug allocation. In Group-A, 90 patients were treated with Itraconazole at a dose of 5 mg/kg/day (study group) and in Group-B 90 patients were treated with Terbinafine at a dose of 3–6 mg/kg/day (control group) for 6 weeks. Erythema, scaling and pruritus were measured initially at baseline and again at the end of the 3rd and 6th week of drug administration. The overall reduction of mean erythema, scaling and pruritus from baseline to the 2nd follow-up of drug administration was more in Itraconazole group than Terbinafine group and it was statistically significant ($p < 0.001$, $p=0.003$ and $p=0.001$, respectively). The cure rate was 62.20% in Itraconazole group and 28.90% in Terbinafine group. Two weeks after cure, the relapse rates were 8.93% and 30.77%, respectively in the Itraconazole and Terbinafine groups. The findings of the study showed that Itraconazole is a better antifungal drug in comparison to Terbinafine ($p < 0.05$).

Keywords: Cutaneous Dermatophytosis, Fungal Infection, Itraconazole, Terbinafine

Introduction

Superficial fungal infections are common skin diseases that affect millions of people worldwide. Approximately 90% of the superficial fungal skin infections are caused by dermatophytes [1]. Dermatophytes are a group of pathogenic fungi responsible for the commonest fungal infection in humans, namely dermatophytosis or tinea [2]. The prevalence of dermatophytosis varies between 13% and 49% depending on the geographical distribution of the countries [3]. Dermatophytosis has several distinct cutaneous manifestations [4]. Recurrent dermatophytic infections cause significant distress to the patients, socially, emotionally and financially. Over the last 3–4 years, the frequency of such cases has increased alarmingly [1, 5]. The dermatophytosis cases

seen in hospitals represent just the tip of the iceberg of the epidemic that is in the community [6, 7].

Pharmacological therapy is effective in dermatophytosis and lowering morbidity in most patients [8]. Various systemic antifungals have been used for dermatophytosis with the initial use of Griseofulvin introduced in the 1950s transcending to Ketoconazole, Fluconazole, Terbinafine and Itraconazole, over the next decade [9]. Effective penetration of the systemically administered drug into the stratum corneum and its persistence (a function of its affinity for keratin or keratin adherence) is an important factor for achieving cure. Terbinafine is an allylamine antifungal, discovered in 1983. Due to the presence of tertbutyl acetylene substitution of the phenyl ring on the side chain of the molecule, Terbinafine interfere in the biosynthesis of fungi. By inhibiting the squalene epoxidase, it stops the formation of ergosterol, with the help of these steps squalene convert into 2,3-oxidosqualene (an ergosterol precursor). So ultimately the growth is stopped in lack of ergosterol and lead a cell death because of weak cell wall integrity. Recent data show that Terbinafine, once a highly effective drug, has a cure rate of 30.6% in tinea corporis, tinea cruris and tinea faciei when given orally at a dose of 5 mg/kg/day for 4 weeks [10].

On the other hand, Itraconazole is an oral synthetic dioxolane triazole compound that inhibits the cytochrome P-450-dependent 14-alpha-demethylation step in the formation of ergosterol. This leads to alterations in a number of membrane associated cell functions. In patients with recurrent cutaneous dermatophytosis, Itraconazole rather than Terbinafine may be particularly useful. Itraconazole is also delivered to the skin as result of passive diffusion from the plasma to the keratinocytes, with strong drug adherence to keratin. This accounts for its persistence in the stratum corneum for 3-4 weeks after discontinuation of therapy. Besides this, Itraconazole has an outstanding pharmacokinetic and pharmacodynamic profile [11, 12].

Terbinafine has been effectively used for dermatophytosis over past three decades due to its favorable mycological and pharmacokinetic profile. 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 [13]. No definite clinical case of Itraconazole resistance has been reported in dermatophytosis, but the Terbinafine resistance rate is 32% [10, 14, 15]. Due to widespread resistance to Terbinafine as antifungal agent against dermatophytosis and a high relapse rate when used in conventional doses, there is a need to find an effective first-line therapy for the management of dermatophytosis to achieve the maximum results with fewer relapses. The data generated from the study might be useful for dermatologists, medicine specialists and physicians in general for the management of dermatophyte infections.

Methods and materials

A randomized controlled trial was conducted in the Department of Pharmacology & Therapeutics at Rajshahi Medical College in collaboration with department of Dermatology and Venereology, at Rajshahi Medical College Hospital, Rajshahi and Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. The study was carried out over a period of 1 year, from July 2021 to June 2022. The cutaneous dermatophytic patients (tinea corporis, tinea capitis, tinea cruris, tinea pedis, tinea barbae, tinea manuum, tinea faciei) of either sex with the age range of 18-60 years were the study population. The study population was divided into 2 groups according to random allocation of drugs by a simple lottery method. Group A Patients got the Itraconazole drug and Group B patients got the Terbinafine drug in the lottery. Patients with proven dermatophyte infection of the skin–confirmed clinically and by scraping with KOH mount were included in the study. Patients with Dermatophyte infection in nails (Tinea unguium), patients on oral treatment of dermatophytosis within last 1 month and on application of topical treatment within the last 2 weeks during the time of data collection, patients had comorbid conditions such as diabetes, hypertension, chronic or active liver disease, low renal function, congestive heart failure which might alter the time frame for treatment with Terbinafine and Itraconazole, Pregnant women and had a lactating baby, underlying keratinization disorders, atopy and hypercortisolism that might complicate dermatophytosis, patients under 1medications such as statins, astemizole, quinidine, terfenadine, ergot alkaloids anticoagulants, patients under immunomodulatory, anti-retroviral, anti-depressants and anti-epileptics drugs and patients had inability to come for follow-up every 3 weeks were excluded. The sample size at 5% level of significance at 80% power were calculated and found 77 in each group. However, considering an estimated 10% drop-out during 6 months' and to ensure more validity of the study findings, a total of 180 patients were included in the study and were randomly assigned to the Itraconazole and Terbinafine groups. Systematic random sampling technique was used to select 180 study subjects who fulfilled the selection criteria.

Study procedure:

A total of 180 patients who met the eligibility criteria were recruited in the study. All patients within the age group of 18-60 years who were diagnosed by the dermatologist (both clinically and KOH examination) as suffering from cutaneous dermatophytosis were included in the study. After informed written consent, the patient's history like age, sex, family history, past history of infection and treatments, duration of current infection and associated disorders were obtained and recorded in the data-sheet. The patients were examined by the designated physicians and they were evaluated on the basis of three parameters: Erythema, scaling and pruritus. Each parameter was graded on a 4-point scale (0=absent, 1=mild, 2=moderate and 3=severe). Erythema and scaling were scored by the dermatologist while pruritus was graded with a 10 cm long visual analog scale under the direct supervision of the dermatologist (Score 0 on the visual analog scale=absent, scores 1-3=mild, 4-7=moderate and 8-10=severe) [16].

Patients were randomly allocated into groups A and B for allotment of the respective drugs. Out of the 180 patients, 90 treated with Itraconazole 5 mg/kg/day (study group) for 6 weeks and the other 90 treated with Terbinafine 3–6 mg/kg/day (control group) for 6 weeks orally, which was prescribed by the consulting physician depending upon age of the patients. Patients were instructed to consult the physician immediately if any unusual side effects (nausea, abdominal pain, vomiting, diarrhea, appetite changes and headache) occur before the follow-up date.

They were followed up at three-week interval after the completion of treatment and 2nd follow-up was given three weeks after the first follow up. During each visit, the scores

of erythema, scaling and pruritus were calculated as mentioned above and recorded for statistical analysis. Any reported adverse drug reactions were also noted. The KOH examination and liver function tests were done at the time of enrolling the patient and at the end of the sixth week. The therapeutic safety and efficacy were evaluated after completion of treatment. Patients were considered cured, when there were no signs and symptoms (scaling, erythema and pruritus) and a negative KOH. Data were collected by using a semi-structured (a research instrument) questionnaire containing all the variables of interest.

Statistical analysis:

Data were processed and analyzed using SPSS (Statistical Package for Social Sciences), version 24. Qualitative variables were described by frequency and percentage, while quantitative variables were described by the mean and standard deviation. Statistical tests were used to analyze the data. A p-value < 0.05 was considered statistically significant for all tests.

Ethical Issues:

Permission was taken from the Institutional Review Board (IRB) of Rajshahi Medical College (RMC), Rajshahi before data collection. Keeping compliance with the Helsinki Declaration for Medical Research Involving Human Subjects 1964, last amended in 2013, all the study subjects were informed verbally about the study design, the purpose of the study and potential benefits expected to be derived from and risks involved in the study. They would have the full rights to withdraw themselves from the study at any time for any reasons what-so-ever. Patients who voluntarily gave informed consent to participate in the study were only included in the study.

Results

Table 1: Distribution of the patients by age (n=90 in each group)

Age in years	Itraconazole group	Terbinafine group
	Frequency (%)	
< 25 years	27 (30.00%)	49 (54.40%)
25-34 years	26 (28.90%)	13 (14.40%)
35-44 years	23 (25.60%)	12 (13.30%)
> 45 years	14 (15.60%)	16 (17.80%)
$\bar{X}$±SD	32.48±11.22 years	29.20±12.36 years

Table 1 revealed that majority of the patients were < 25 years old, in the Itraconazole group, 30.00% of the patients were < 25 years old and in the Terbinafine group, 54.40% of the patients were < 25 years old. The mean age of the patients in the Itraconazole group was 32.48±11.22 years and in the Terbinafine group it was 29.20±12.36 years.

Table 2: Distribution of the patients on the basis of occupational status (n=90 in each group)

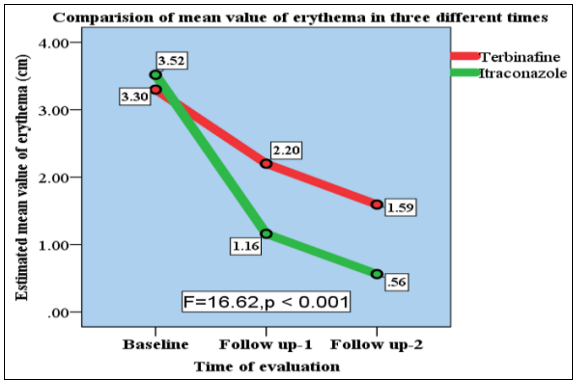
Occupational status	Itraconazole group	Terbinafine group
	Frequency (%)	
Farmer	2 (2.20)	3 (3.30)
Service holder	4 (4.40)	3 (3.30)
Businessman	6 (6.70)	8 (8.90)
Student	20 (22.20)	32 (35.60)
Housewife	58 (64.40)	44 (48.90)
Total	90 (100%)	90 (100%)

Table 2 showed the occupational status of the patients. It revealed that the majority of the patients were housewives in both group, in the Itraconazole group 64.40% of the patients were housewives, in the Terbinafine group, 48.90% of the patients were housewives.

Table 3 showed the duration of the disease for the patients. It revealed that in the Itraconazole group, majority 64.40% of the patients suffered from dermatophytosis of <6 months duration and similarly, in the Terbinafine group, most 77.80% of the patients suffered from the condition < 6 months.

Table 3: Distribution of the patients on the basis of duration of the disease (n=90 in each group)

Duration of disease (month)	Itraconazole group	Terbinafine group
< 6 month	58 (64.40%)	70 (77.80%)
≥ 6 month	32 (35.60%)	20 (22.20%)



Source: Data were analyzed with Repeated Measure ANOVA statistics and were presented as mean ± SD

Fig 1: Monitoring of erythema at different time interval

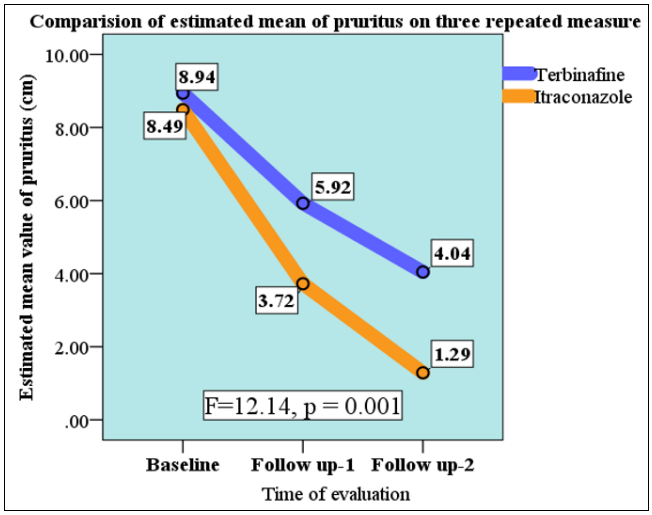
Fig 1 showed the evaluation of erythema at three different times. It revealed that in the Itraconazole group, the mean erythema at baseline was 3.52 cm, which decreased to 1.16 cm at the 1st follow-up and then to 0.56 cm at the 2nd follow-up of drug administration. On the other hand, in the Terbinafine group, the mean erythema at baseline was 3.30 cm which decreased to 2.20 cm at the 1st follow-up and then to 1.59 cm at the 2nd follow-up of drug administration. The overall reduction of erythema from baseline to the 2nd follow-up of the intervention between the two drugs was statistically significant ($p < 0.001$).

Table 4: Monitoring of scaling at different time interval

Time of evaluation	Itraconazole group	Terbinafine group	F, p-value#
	mean ± SD (cm)		
At baseline	4.95±1.70	4.97±1.93	9.09, 0.003
At 1st follow-up	1.57±0.87	2.90±1.60	
At 2nd follow-up	0.57±0.20	2.06±0.73	

Source: Data were analyzed with Repeated Measure ANOVA statistics and were presented as mean ± SD

In the Itraconazole group, the mean scale at baseline was 4.95±1.70 cm which decreased to 1.57±0.87 cm at the 1st follow-up and then to 0.57±0.20 cm at the 2nd follow-up of drug administration. On the other hand, in the Terbinafine group, the mean scaling at baseline was 4.97±1.93 cm, which decreased to 2.90±1.60 cm at the 1st follow-up and then to 2.06±0.73 cm at the 2nd follow-up of drug administration. The overall reduction of scaling from baseline to the 2nd follow-up of intervention between the two drugs was statistically significant ($p = 0.003$).



Source: Data were analyzed with Repeated Measure ANOVA statistics and were presented as mean ± SD

Fig 2: Monitoring of pruritus at different time interval

Fig 2 showed the evaluation of pruritus at three different times. In the Itraconazole group, the mean pruritus at baseline was 8.49 cm, which decreased to 3.72 cm at the 1st follow-up and then to 1.29 cm at the 2nd follow-up of drug administration. On the other hand, in the Terbinafine group, the mean pruritus at baseline was 8.94 cm which decreased to 5.92 cm at the 1st follow-up and then to 4.04 cm at the 2nd follow-up of drug administration. The overall reduction of pruritus from baseline to the 2nd follow-up of intervention between the two drugs was statistically significant ($p = 0.001$).

Table 5: Comparison of percent of reduction of erythema, scaling and pruritus from baseline to 2nd follow-up between the two groups

Time of evaluation	Itraconazole group	Terbinafine group	t, p-value#
	mean ± SD (cm)		
Erythema	83.49±17.25	34.79±19.22	4.13, < 0.001
Scaling	80.31±15.55	44.97±17.43	3.33, 0.001
Pruritus	84.79±13.90	50.90±15.05	4.42, < 0.001

Source: Data were analyzed with an **Independent sample t test** and were presented as mean ± SD

Table 5 showed the percent of reduction of erythema, scaling and pruritus between the two groups. It revealed that in case of erythema the percent of reduction from baseline in the Itraconazole group was 83.49±17.25 and in the Terbinafine group it was 34.79±19.22 and it was statistically highly significant ($p < 0.001$). In scaling the percent of reduction in the Itraconazole group was 80.31±15.55 and in the Terbinafine group it was 44.97±17.43 and it was statistically significant ($p=0.001$). In the case of pruritus, the percent of reduction from baseline in the Itraconazole group was 84.79±13.90 and in Terbinafine group it was 50.90±15.05 and it was also statistically highly significant ($p < 0.001$). It indicates that Itraconazole was very effective in comparison to Terbinafine.

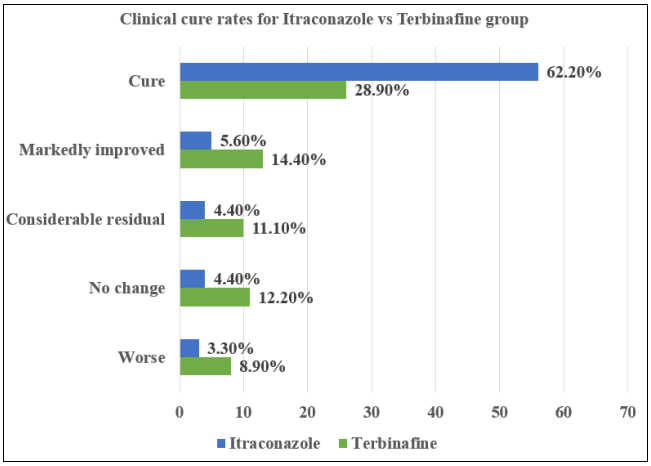


Fig 3: Clinical cure rates for Itraconazole vs Terbinafine group (n=90 in each group)

In the Itraconazole group, more than 3/5th (62.20%) of the patients were cured, 5.60% were markedly improved, 4.40% had considerable residual, 4.40% had no change and 3.30% developed worse conditions from baseline. In the Terbinafine group, more than 1/4th (28.90%) of the patients were cured, 14.40% were markedly improved, 12.20% had no change, 11.10% had considerable residual and 8.90% developed worse conditions from baseline.

Table 6: Distribution of patients on the basis of overall side effects in 2nd follow-up (Itraconazole group=72, Terbinafine group=68)

Side effects	Itraconazole group	Terbinafine group	df	χ^2 p value
	Frequency (%)			
Yes	11 (36.70)	19 (63.30)	1	3.33 0.07
No	61 (55.50)	49 (44.50)		

(N.B.-in the 2nd follow-up, 12 patients in the Itraconazole group and 22 patients in the Terbinafine group dropped out after the 1st follow-up.)

On the basis of overall side effects in the 2nd follow-up, it was revealed that in the Itraconazole group, 11 (36.70%) patients had side effects and 61 (55.50%) did not. On the other hand, in the Terbinafine group, 19 (63.30%) patients had side effects and 49 (44.50%) did not and there was no statistically significant difference in terms of side effects in the 2nd follow-up between the two groups (p=0.07).

Table 7: Relapse rates 2 weeks after cure in Itraconazole and Terbinafine group (Itraconazole group=56, Terbinafine group=26)

	Itraconazole	Terbinafine
Number of patients cured	56	26
Number of patients with relapse	5	8
Total number of patients relapsed (%)	8.93%	30.77%

(Only cured patients were considered here) $\chi^2 = 4.82$, df=1, p=0.02

After 2 weeks of completion of treatment, only 5 (8.93%) of patients relapsed in the Itraconazole group and less than 1/3rd (30.77%) of patients relapsed in the Terbinafine groups. The relapse rate was higher in Terbinafine group in comparison to Itraconazole group and it was statistically significant (p=0.02).

Discussion

In the present study, the mean age of the patients in the Itraconazole group was 32.48±11.22 years and in the Terbinafine group was 29.20±12.36 years. A study done by Brigida and Elizabeth, (2021) in India found that the mean age of the subjects in the Itraconazole group was 27.3 ± 8.3 years, which was nearly similar to our findings, but in the Terbinafine group was 39.2±13.2 years which was much higher than our study findings [15]. Brigida and Elizabeth, (2021) showed that the majority of subjects in Terbinafine group were in the age group of 31 to 40 years (30%) but in our study the majority (54.40%) of the patients were < 25 years, whereas the majority of subjects in the Itraconazole group were in the age group of 21 to 30 years (48%) and in our study 30% of the patients were < 25 years, which was partially similar to our findings [15]. Rahim, (2012) found that dermatophytosis was more common in the age group of 21-30 years, which was partially similar to our study findings, where in both groups a large portion of respondents were below 25 years of age [1]. Another study done by Dhoot *et al*, (2020) found that the average age of the patients was 38.28 and 33.25 years, respectively, in Itraconazole and Terbinafine groups which findings were nearly similar to our study findings [16]. Increased participation in outdoor physical activity, increased sweating, increased exposure to wet work and shoe wearing habits responsible for dermatophytosis in the age group 21-30 years in study by Rahim, (2012) [1].

In the present study, the majority (64.40%) of the patients suffered from dermatophytosis had < 6 months' duration and 35.60% suffered from ≥ 6 months in the Itraconazole group. Similarly, in the Terbinafine group, majority (77.80%) of the patients suffered from < 6 months and 22.20% suffered from ≥ 6 months. Brigida and Elizabeth, (2021) in their study reported that in the Terbinafine group, the duration of the disease was < 6 months among 84% of subjects and 8% had > 6 months' duration. In Itraconazole group, 86% of subjects had the disease for < 6 months and 14% > 6 months. These findings were nearly similar to our study findings [15].

In the present study, in the Itraconazole group, the mean erythema at baseline was 3.52 cm, which decreased to 1.16cm at the 1st follow-up and then to 0.56cm at the 2nd follow-up of drug administration. On the other hand, in the Terbinafine group, the mean erythema at baseline was 3.30cm, which decreased to 2.20cm at the 1st follow-up and then to 1.59cm at the 2nd follow-up of drug administration. The overall reduction of erythema from baseline to the 2nd follow-up of intervention between the two drug was statistically significant (p < 0.001). Similarly, the overall reduction of scaling from baseline to the 2nd follow-up of intervention between the two drug was statistically significant (p = 0.003). Also the overall reduction of pruritus from baseline to the 2nd follow-up of intervention between the two drugs was statistically significant (p = 0.001). Dhoot *et al*., (2020) in India reported that there was a statistically significant improvement (p value <0.05) in the total symptom score (erythema, scaling, and pruritus) in Itraconazole as well as in Terbinafine compared to baseline. The significant improvement started from 0-2 weeks and then persisted till the end of the treatment in both groups [16].

In the present study, in the Itraconazole group, the majority (62.20%) of the patients was cured, 5.60% were markedly improved, 4.40% had considerable residual, 4.40% had no change and 3.30% developed worse conditions from baseline. In the Terbinafine group, 28.90% of the patients were cured, 14.40% were markedly improved, 12.20% had no change, 11.10% had considerable residual and 8.90% developed worse condition from baseline. A study done by Koregol *et al*., (2021) in India reported that the response to Itraconazole was 72.2% and Terbinafine was 42.2% which findings were nearly similar to our study findings [5]. Similar findings also found in a study done by Havu *et al*. (2000) [17]. They reported that at the end of 12 weeks, there were only 43 cases out of the total 100 cases enrolled who were able to maintain a long- term clinical and mycological cure after 2 weeks of oral Terbinafine treatment. They also concluded that incomplete mycological cure was very common after standard (2 weeks) Terbinafine therapy in patients with dermatophytosis (Havu *et al*., 2000) [17]. Similar of our findings were also found in a study done by Bhatia *et al*., (2019) in India, where Itraconazole has higher clinical and mycological cure rates as compared to terbinafine [18]. Another study done by Brigida and Elizabeth, (2021) in India showed that mycological cure was better in the Itraconazole group (88%) compared to the Terbinafine group (70%) [15]. Similar findings also found in a study done by Singh *et al*., (2018) where Itraconazole was more effective than Terbinafine [10].

But Dhoot *et al*., (2020) found that at the end of four weeks, the clinical cure rate was significantly better in the Terbinafine group as compared to the Itraconazole group but no statistical difference was observed at the end of six weeks which findings were not similar to our study [16]. Our contradictory findings were also found in a study done by Kovitwanichkanont and Chong, (2019), where Terbinafine was superior to Itraconazole for both clinical and mycological cure of dermatophytosis [19]. Another study done by Amit *et al*., (2013) in India reported that the cure rate of Terbinafine was 87% [20]. This cure rate was very high in comparison to our findings and might be due to the fact that this study was conducted about 9 years ago. After 2 weeks of completion of treatment, only 8.93% of patients

relapsed in the Itraconazole group and 30.77% of patients relapsed in the Terbinafine groups and it was statistically significant (p=0.02). The relapse rate was higher in the Terbinafine group in comparison to Itraconazole group. Singh *et al*., (2019) reported that at 4 weeks, 2 and 1 patients relapsed in the Itraconazole and Terbinafine groups, respectively (p=0.420). Relapse rates after 8 weeks of cure in different groups were not significantly different [10].

Conclusion

Our study revealed that Itraconazole is a better antifungal drug than Terbinafine. Further studies, including multicenter and larger sample size, are recommended.

References

1. Rahim MR, Saleh AA, Miah MRA, Anwar S, Rahman MM. Pattern of dermatophyte in Bangabandhu Sheikh Mujib Medical University. Bangladesh Journal of Medical Microbiology. 2012; 6(2):11-14.
2. George FF, Muhaj SJ, Tyring SK. Bacterial antimicrobial resistance and dermatological ramifications. Journal of Dermatology. 2019; 187(1):12-20.
3. Kakande T, Batunge Y, Eilu E, Shabohurira A. Prevalence of dermatophytosis and antifungal activity of ethanolic crude leaf extract of Tetradenia riparia against dermatophytes isolated from patients. Dermatology Research and Practice. 2019; 50(2):1-13.
4. Kumar MP, Chaudhary A, Singh MA, Soni A. Preformulation study of itraconazole for novel drug delivery system fromulation. European Journal of Biomedical and Pharmaceutical sciences. 2020; 8(9):488-494.
5. Koregol SC, Naik SR, Hosthota A, Koregol AC. A comparative study of efficacy of oral itraconazole, terbinafine and fluconazole: A clinical trial. International Journal of Research in Dermatology. 2021; 7(3):435.
6. Shakya NB, Jha SM, Dangol A, Shakya S, Shah A. Efficacy of itraconazole versus terbinafine for the treatment of tinea cruris. Medical Journal of Shree Birendra Hospital. 2013; 11(1):24-26.
7. Bishnoi A, Vinay K, Dogra S. Emergence of recalcitrant dermatophytosis in India. The Lancet Infectious Diseases. 2018; 18(3):250-251.
8. Aftab BT, Dobromilskaya I, Liu JO, Rudin CM. Itraconazole Inhibits Angiogenesis and Tumor Growth in Non–Small Cell Lung Cancer. Cancer Research. 2011; 71(21):6764-6772.
9. Dogra S, Uprety S. The menace of chronic and recurrent dermatophytosis in India: Is the problem deeper than we perceive? Indian Dermatology Online Journal. 2016; 7(2):73-76.
10. Singh A, Masih A, Khurana A, Singh PK, Gupta M, Hagen F, *et al*. High terbinafine resistance in Trichophyton interdigitale isolates in Delhi, India harbouring mutations in the Squalene epoxidase (SQLE) gene. Mycoses. 2018; 61(7):477-484.
11. Schueller O, Willson A, Singh N, Lohmer L, Alabanza A, Patel J. A phase 1 pharmacokinetic drug interaction study of belumosudil coadministered with CYP3A4 inhibitors and inducers and proton pump inhibitors. Clin. Pharmacol. Drug Dev. 2022; 11:795-806.
12. Balakumar S, Rajan S, Thirunalasundari T. Epidemiology of dermatophytosis in and around Tiruchirapalli, Tamilnadu, India. Asian Pacific Journal of Tropical Disease. 2012; 2:286-289.
13. Majid I, Sheikh G, Kanth F, Hakak R. Relapse after oral terbinafine therapy in dermatophytosis: A clinical and mycological study. Indian Journal of Dermatology. 2016; 61(5):529-533.
14. Sardana K, Kaur R, Arora P, Goyal R, Ghunawat S. Is Antifungal Resistance a Cause for Treatment Failure in Dermatophytosis: A Study Focused on Tinea Corporis and Cruris from a Tertiary Centre? Indian Dermatology Online Journal. 2018; 9(2):90-95.
15. Brigida S, Elizabeth AA. A comparative study of efficacy of oral terbinafine and oralitraconazole in tinea corporis / tinea cruris infection. Journal of Pharmaceutical Research International, 2021, 94-105.
16. Dhoot D, Shah B, Shah S, Jangid N, Deshmukh G. Comparative evaluation of efficacy and safety of terbinafine and itraconazole in the management of tinea corporis et cruris. IP Indian Journal of Clinical and Experimental Dermatology. 2020; 6(3):231-236.
17. Havu V, Heikkilä H, Kuokkanen K, Nuutinen M, Rantanen T, Saari, S, *et al*. A double-blind, randomized study to compare the efficacy and safety of terbinafine (Lamisil) with fluconazole (Diflucan) in the treatment of onychomycosis. The British Journal of Dermatology. 2000; 142(1):97-102.
18. Bhatia A, Kanish B, Badyal DK, Kate P, Choudhary S. Efficacy of oral terbinafine versus itraconazole in treatment of dermatophytic infection of skin - A prospective, randomized comparative study. Indian Journal of Pharmacology. 2019; 51(2):116-119.
19. Kovitwanichkanont T, Chong AH. Superficial fungal infections. Australian Journal of General Practice. 2019; 48(10):706-711.
20. Amit K, Navin B, Priyamvada S, Monika S. A comparative study of efficacy of terbinafine and fluconazole in patients of tinea corporis. Int. J. Pharm. Med. & Bio. Sc. 2013; 2(4):92-98.