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Original Research Article

A Comparative Evaluation of the Efficacy of Oral Terbinafine versus Itraconazole in the Treatment of Dermatophytosis

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Abstract

Background: Dermatophytic infections, often worsened by hot and humid climates, are common fungal infections. Terbinafine and itraconazole are widely used oral antifungal agents to treat these conditions. However, increasing resistance to these drugs at conventional doses and durations has been observed. Consequently, this study was designed to compare the efficacy of terbinafine and itraconazole when administered in treating tinea corporis and tinea cruris.

Methods: A randomized, prospective comparative study was conducted, involving 80 newly diagnosed patients with tinea corporis and tinea cruris, aged 18 years and above. The clinical diagnosis was confirmed using a potassium hydroxide (KOH) test. Patients were divided into two groups: Group I and Group II. Group I received oral itraconazole 100 mg twice daily, while Group II received oral terbinafine 250 mg twice daily, both treatments lasting for six weeks. Patients were followed up at the 2nd, 4th, and 6th weeks.

Results: The mean age of patients of group I and group II cases was 38.19 ± 13.5 and 35.28 ±13.5 years respectively. Most cases (78.75%) involved both tinea corporis and tinea cruris, indicating a combined presentation. Tinea corporis was the second most common diagnosis, accounting for 10% of cases. Tinea cruris was the least common diagnosis, representing 11.25% of cases. Both groups experienced noticeable improvements in the presence of erythema. Group II showed significant improvement in scaling as compared to group I as shown by significant p values at the end of the second follow up and third follow up. The pruritus scores were substantially improved in group II indicating faster resolution. It appears that both medications are capable of improving clinical symptoms related to dermatophytosis.

Conclusion: Both itraconazole and terbinafine are effective treatment options for the treatment of dermatophytosis. However, terbinafine appears to offer superior efficacy in addressing scaling and pruritus, especially in the early stages of treatment. The incidences of adverse drug reactions were low in both groups and both medications were well tolerated.

Keywords: Dermatophytosis, Efficacy, Terbinafine, Itraconazole.

Introduction

Dermatophytes are a group of filamentous fungi which have keratin as the source of nutrition. Dermatophyte infection is described by a condition known as dermatophytosis. Dermatophytes can affect the skin leading to cutaneous changes that appear ring-shaped with a clear center and red margin which is why it is referred to as ringworm [1, 2]. Skin yeasts are relatively widespread in every age group and both genders of humans [3]. Dermatophyte fungi species that affect humans are Epidermophyton spp., Microsporum spp., and Trichophyton spp. The range of dermatophyte infections has changed apparently throughout the years, but the most significant number of cases is attributed to Trichophyton spp. Among the etiologic agents, Trichophyton rubrum, more often, has kept its leadership in causing dermatophyte infections throughout the century [4]. Itraconazole is a broad-spectrum triazole class antifungal agent which is used to treat different forms of fungal infections. It functions by reducing the ergosterol synthesis which in turn slows the rate of growth of a fungal cell through affecting its cell membrane [5]. Some of the clinical studies conducted on itraconazole have indicated that the drug is effective in the treatment of dermatophytes, candida, and some of the non-dermatophyte molds [6,7]. They said that side effects include

gastrointestinal symptoms which are common while others include rashes/pruritus, hypokalemia, headache, hypotension, leukocytopenia, and reduced renal function [8].

Terbinafine, an allylamine antifungal antibiotic can also be viewed as inhibiting ergosterol synthesis but does this upstream of the ergot inhibit squalene epoxidase? This diminishes the ergosterol level and also the build-up of fatty toxic substance squalene thus leading to death of the fungi. Terbinafine, on the other hand, has less severe side effects and those are usually dose-related and mostly resolve on their own, some of the side effects include sore throat or headaches, stomach upsets, and rashes. As such, terbinafine can be termed to be relatively safer in its usage [9]. The effectiveness of both, itraconazole and terbinafine in the treatment of dermatophyte infections is documented in many papers [10-12]. From an empirical point of view in clinical practice, a question would be raised; which of the two drugs is more effective in general and standard clinical cases? Hence the present study is being undertaken to compare the clinical effectiveness of oral itraconazole 100 mg bd and terbinafine 250 mg bd in the management of dermatophytic skin infections under a tertiary care teaching hospital located in South India.

Material and Methods

This prospective comparative study was conducted in the Department of Dermatology in collaboration with the Department of Pharmacology, Govt Medical College and Hospital, Mahabubabad, Telangana State. Institutional Ethical approval was obtained for the study. Written consent was obtained from all the participants of the study after explaining the nature of the study in vernacular language.

Inclusion Criteria

1. Freshly diagnosed patients of aged 18 years and above with clinical diagnosis of tinea corporis and tinea cruris confirmed by potassium hydroxide (KOH) test.
2. Attending Dermatology OPD at our Medical College Hospital.
3. Males and Females.
4. Willing to participate in the study voluntarily.

Exclusion Criteria

1. Patients with a history of Hepatic diseases
2. Patients with a history of renal disease
3. Patients with a history of cardiovascular disease
4. Pregnant and lactating women.

A randomized, prospective comparative study was conducted, involving a total of 80 newly diagnosed patients with tinea corporis and tinea cruris, aged 18 years and above. The clinical diagnosis was confirmed using a potassium hydroxide (KOH) test. Patients were divided into two groups: Group I and Group II. Group I received oral itraconazole 100 mg twice daily, while Group II received oral terbinafine 250 mg twice daily, both treatments lasting for six weeks. Patients were followed up at the 2^{nd}, 4^{th}, and 6^{th} weeks. In Group I, each patient received itraconazole 100 mg twice daily until the lesions resolved or for a maximum of six weeks. In Group II, each patient received terbinafine 250 mg twice daily under the same conditions. During each follow-up visit, clinical responses were assessed in three parameters: scaling, erythema, and pruritus, which were scored on a scale of 0-3 (0 = absent, 1 = mild, 2 = moderate, 3 = severe). A patient was considered cured when there was an absence of scaling, erythema, and pruritus, along with a negative KOH test.

Statistical analysis: All the available data was uploaded to an MS Excel spreadsheet and analyzed by SPSS version 22 in Windows format. The continuous variables were represented as mean, standard deviation, and percentage. Categorical variables were calculated by chi-square test and values of p (<0.05) were considered as significant.

Results

A total of 80 patients were selected as per the inclusion and exclusion criteria and allotted to two groups equally with random allocation using computer-generated random numbers. Group 1 patients were given oral itraconazole 100mg twice daily and group II patients were given terbinafine 250mg twice daily. The demographic profile and diagnosis of patients are shown in Table 1. The study included participants aged 18 to 60 years. The largest age group was 41-50 years, followed by 31-40 years. This indicates that dermatophytosis is more prevalent in middle-aged adults. The distribution of cases between the two age groups was relatively balanced, with Group I have slightly more participants in the younger age groups and Group II having slightly more participants in the older age groups. The mean age of patients was 38.19 ± 13.5 and 35.28 ±13.5 years respectively, Group I had 28 (70%) males and 12 (30%) females, while in Group II there were 26 (65%) males and 14(35%) females.

Table 1: Showing the demographic profile of the cases included in the study.

Age group	Group I (Itraconazole 100mg)	Group II (Terbinafine 250mg)	Total (%)
18 – 30	10 (25.0%)	9 (22.5%)	19 (23.75%)
31 – 40	11 (27.5%)	12 (30.0%)	23 (28.75%)
41 – 50	15 (37.5%)	16 (40.0%)	31 (38.75%)
51 - 60	4 (10.0%)	3 (7.5%)	07 (8.75%)
Total	40 (100.0%)	40 (100.0%)	80 (100.0%)

Figure 1 shows the largest portion of participants in both Group I and Group II, suggesting that dermatophytosis is more prevalent in individuals with manual labor occupations. Other occupational groups, such as skilled workers, clerks, professionals, and students, are represented in relatively balanced proportions across the two groups. There are no significant differences in the occupational distribution between Group I and Group II. The data suggests that dermatophytosis may be more prevalent in individuals engaged in unskilled labor or agricultural activities. This could be due to increased exposure to potential fungal sources or factors related to working conditions.

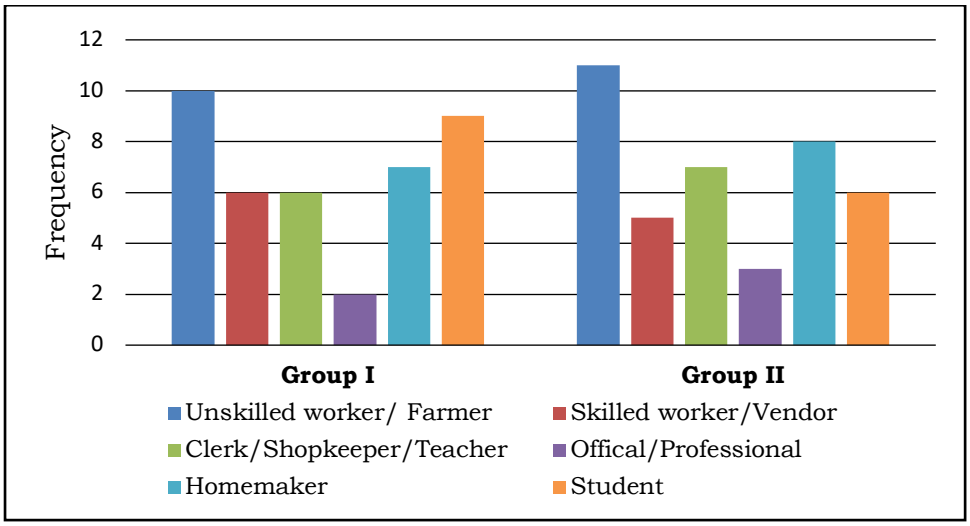

Figure 1: Showing the distribution of cases included in the study based on occupation.

Table 2 presents the diagnosis of dermatophytosis included in the study. Most cases (78.75%) involved both tinea corporis and tinea cruris, indicating a combined presentation. Tinea corporis was the second most common diagnosis, accounting for 10% of cases. Tinea cruris was the least common diagnosis, representing 11.25% of cases.

Table 2: Diagnosis of cases included in the study

Diagnosis	Group I (Itraconazole 100 mg)	Group II (Terbinafine 250 mg)	Total (%)
Tinea corporis	3 (7.5%)	5 (12.5%)	8 (10%)
Tinea cruris	5 (12.5%)	4 (10.0%)	9 (11.25%)
Tinea corporis and cruris	32 (80.0%)	31 (77.5%)	63 (78.75%)
Total	40 (100.0%)	40 (100.%)	(100.0%)

Table 3 presents the baseline clinical parameters for two groups of patients with dermatophytosis: Group I (Itraconazole 100mg) and Group II (Terbinafine 250mg). The parameters evaluated include erythema, scaling, and pruritus. The severity of each parameter is categorized as none, mild, moderate, or severe. Both groups had a similar distribution of erythema severity, with a majority of cases falling into the moderate category. Scaling was more prevalent in Group I (Itraconazole) compared to Group II (Terbinafine). Pruritus was significantly more severe in Group I compared to Group II although all the values were not significant.

Table 3: Clinical parameters in two groups of cases with Dermatophytosis

Baseline	Group I (N=40) (Itraconazole 100 mg)				Group II(N=40) (Terbinafine 250 mg)				P value
	No	Mild	Moderate	Severe	No	Mild	Moderate	Severe	
Erythema	0	2	12	26	0	0	18	22	0.121
Scaling	0	8	28	4	0	6	29	5	0.457
Pruritus	0	2	37	1	0	1	39	0	0.667

The clinical outcomes of two groups of patients with dermatophytosis treated with Itraconazole and terbinafine at different follow-up visits are depicted in Table 4. A critical analysis of the table shows that after the first follow-up visit at the end of the second week. Both groups experienced noticeable improvements in the presence of erythema. Over time the improvement continued to increase. However, there were no major changes in the two cohorts based on the p values. Similarly, group II showed significant improvement in scaling as compared to group I as shown by significant p values at the end of the second follow-up and third follow-up. The pruritus scores were substantially improved in group II indicating faster resolution. It appears that both medications are capable of improving clinical symptoms related to dermatophytosis. However, terbinafine seems to perform better in relieving scaling and pruritus faster than itraconazole.

Table 4: Results of treatment done in two groups at different intervals

First, follow up (2^{nd} week)	Group I (N=40) (Itraconazole 100 mg)				Group II(N=40) (Terbinafine 250 mg)				P value
	No	Mild	Moderate	Severe	No	Mild	Moderate	Severe	
Erythema	1	10	28	1	1	10	26	3	0.554
Scaling	9	27	4	0	5	22	13	0	0.061
Pruritus	0	3	35	2	3	32	3	0	0.334
Second, follow-up (4^{th} week)	No	Mild	Moderate	Severe	No	Mild	Moderate	Severe	
Erythema	8	30	2	0	7	24	9	0	0.112
Scaling	32	7	1	0	22	18	0	0	0.019*
Pruritus	10	21	9	0	3	23	14	0	0.039*
Third follow up (6^{th} week)	No	Mild	Moderate	Severe	No	Mild	Moderate	Severe	
Erythema	30	10	0	0	28	12	0	0	0.251
Scaling	38	2	0	0	32	8	0	0	0.041*
Pruritus	30	8	2	0	23	15	2	0	0.144

*Significant

The study analyzed the adverse effects reported in two groups of patients given in table 5. Gastrointestinal upset was the common adverse effect reported in 6.25% of patients. Rashes and headaches were found to occur in Hypotension was a rare adverse effect, reported in 2.5% of patients. Group I (Itraconazole) had a slightly higher incidence of adverse effects compared to Group II (Terbinafine). All the adverse effects were self-limiting and did not require patients to discontinue the medications. Therefore, both Itraconazole and Terbinafine were generally well-tolerated, with a low incidence of adverse effects.

Table 5: Adverse effects of the medications reported in the study

Diagnosis	Group I(Itraconazole 100 mg)	Group II(Terbinafine 250 mg)	Total (%)
GI upset	4 (10.0%)	2 (5.0%)	6 (15.0%)
Rashes/	1 (2.5%)	0 (0.0%)	1 (2.5%)
Headaches	3 (7.5%)	2 (5.0%)	5 (12.5%)
Hypotension	2 (5.0%)	0 (0.0%)	2 (5.0%)
Total	10 (25.0%)	4 (10.0%)	14 (35.0%)

Discussion

Skin infections caused by a group of fungi known as dermatophytes affect the superficial layers of the skin. Both topical and oral antifungal medications are crucial in managing these infections. Triazoles, specifically itraconazole, are frequently used

antifungals and have demonstrated marked efficacy against dermatophyte infections [12]. Various scientific investigations have looked at the effectiveness of itraconazole and terbinafine for the treatment of dermatophytic infections [14-16]. There is still an ongoing argument about whether of these two therapies is better and what the most beneficial medication regimen should be with respect to achieving the top results while minimizing side effects. There is a tendency for an increase in the prevalence of dermatophytosis and resistance to conventional anti-fungal drugs in recent times as noted by diminished or failed response to the standard treatment. Earlier topical antifungals were considered as first-line drugs in the management of dermatophytosis. However, the present clinical trials show that patients with large and multisite dermatophytosis often fail to respond to the treatment. These are the cases where systemic therapy is recommended. Terbinafine is a systemic fungicidal drug active against dermatophytes. Fungistatic drugs includes griseofulvin, Itraconazole, and fluconazole [17, 18]. Generally, terbinafine and itraconazole are more commonly prescribed because griseofulvin and fluconazole have longer treatment duration for cure [19]. In this study, we used these two agents to determine the efficacy of treatment in cases of dermatophytosis patients reporting to our center. In this study, we found that both Itraconazole and Terbinafine were effective in treating dermatophytosis. Terbinafine demonstrated superior efficacy in addressing scaling and pruritus, especially in the early stages of treatment. For erythema, both medications showed similar effectiveness. In the past, Terbinafine, dose of 250 mg/day, has shown consistent efficacy against dermatophytosis, achieving more than 90% cure rates at a dose of 250 mg/day when administered for two weeks [20, 21]. However, recently, an increase in the incidence of terbinafine resistance has resulted in treatment failure [22]. Although resistance to terbinafine in dermatophytosis is not common in clinical practice, it has been reported in clinical isolates by a few authors [20-23]. However, in this study, we found acceptable cure rates with both medications with standard dosages. In the current study, we found that both Itraconazole and Terbinafine are effective in treating dermatophytosis. However, Terbinafine may be more effective in addressing scaling and pruritus. The findings of other studies on patients with tinea cruris have reported higher cure rates with itraconazole compared to terbinafine [23]. Other studies on toenail onychomycosis have shown that terbinafine is more effective than itraconazole [24]. Since both drugs have similar pharmacokinetic profiles, our study did not find any significant difference in their efficacy. Although better results were observed in the terbinafine group in the initial stages of follow-up overall outcomes remained similar. The comparison of the safety profile of both drugs also has shown that terbinafine has lower incidences of adverse drug reactions as compared to itraconazole although statistical significance was not found.

Conclusion

Within the limitations of the current study, we conclude that both itraconazole and terbinafine are effective treatment options for the treatment of dermatophytosis. However, terbinafine appears to offer superior efficacy in addressing scaling and pruritus, especially in the early stages of treatment. The incidences of adverse drug reactions were low in both groups and both medications were well tolerated. Further research is needed to explore the long-term effects of these medications and to identify optimal treatment strategies for different patients.

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