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A Comparative Study of Efficacy of Oral Terbinafine and Oralitraconazole in Tinea Corporis / Tinea Cruris Infection

S. Brigida[1] and Arul Amutha Elizabeth[1*]

[1]Department of Pharmacology, Sree Balaji Medical College and Hospital (Affiliated to Bharath Institute of Higher Education and Research), Chennai, Tamil Nadu, India.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Dermatophytoses which are superficial fungal infections of the skin, hair, and nail are among the most common infective dermatoses seen in dermatology outpatient clinics. Today, we are facing an onslaught of chronic and recurrent dermatophytosis in volumes never encountered previously. Itraconazole was found to be the better antifungal in terms of clinical cure,mycological clearance and less need for extension of treatment than Terbinafine. Overall, oral Itraconazole 200 mg/day for 2 weeks proved to be a better agent with excellent and significantly better cure rates than oral Terbinafine 500mg/day for 2 weeks. With Itraconazole, the contra-indications, drug interactions must be kept in mind to prevent loss of efficacy/ potentially hazardous interactions. Both drugs had a good safety profile and few minor adverse events. The reasons for extension of treatment comprise chronicity, previous treatment with OTC steroid preparations, and misuse of systemic antifungal drugs, diabetes, and obesity. Poor personal practices and hygiene also havetheir contribution. Significant associations were also noted between diabetes and chronicity.

**Corresponding author: E-mail: arulamutha@bharathuniv.ac.in;*

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1. INTRODUCTION

Superficial dermatophytosis affecting skin, hair and nail are among the most common public health problem in countries like India, given the tropical climatewith heat and humidity. Cutaneous dermatomycoses are mostly caused by keratinophilic filamentous fungi called dermatophytes and are classified into three genera: *Trichophyton*, MicrosIporum and EpidermIophyton. So far, about 30 species of dermatophytes have been identified as human pathogens [1]. World Health Organization estimates that dermatophytes affect about 25% of the world population [2]. It is also estimated that 30 to 70% of adults are asymptomatic carriers of these pathogens and that the incidence of this disease increases with age [2]. The estimated lifetime risk of acquiring dermatophytosisis between 10 and 20 %3.The epidemiology and distribution of dermatophytosis are influenced by many factors including climate, race, sex, population migration, socialpractices and beliefs, host factors and agent factors [3].

The most common dermatophytes that cause superficial cutaneous mycoses are *Trichophyton rubrum, Trichophyton mentagrophytes, Epidermophyton floccosum* [4]. The dermatophytes, though similar in their morphology, are capable of producing a varied spectrum of clinical manifestations affecting different sites on the skin surface. The nature of the affecting species, its pathogenicity, and the enzyme profile could be responsible in producing a variety of clinical diseases. Although dermatophyte- infections are generally limited to the upper layers of the skin, these fungi can behave in an invasive manner, causing deep and disseminated infection, especially in immunocompromised patients [5]. In the majority of patients, the infection tends to be short-lived, whereas in others it runs a chronic course usually with remissions and exacerbations. Such patients remain as reservoirs of infection and spread the disease to their family members and eventually to the community.

Amongst clinical cases of *T. pedis, T. corporis* and *T. cruris*, the most frequently isolated species is the anthropophilic dermatophyte *T. rubrum*. *T. rubrum* accounted for 76 percent of all superficial fungal diseases in a representative sample of the U.S. population [6].Epidemiological studies on the occurrence of dermatophytes have also shown that *T. rubrum* is present in 80% of cases and *T. mentagrophytes* in 20% [7]. Mycoses has been associated with significant negative social, psychological, and occupational health effects that can compromise the quality of life. Early recognition and treatment is essential to reduce morbidity and possibility of transmission. Many studies have been conducted on chronic dermatophytosis [8-10].

Chronic dermatophytosis was defined as refractory dermatophytosis which runs a chronic course with episodes of remissions and exacerbations, with or without treatment. Treatment of dermatophytosis is generally prolonged and expensive. Dermatophytosisis often associated with relapses following irregular antifungal therapy. Recently, clinical failure has been observed in patients treated with antifungal and drug resistance has become an important problem. The traditional treatment of Dermatophytosis has been with Griseofulvin and Ketoconazole, and they are not the drug of choice today, due to significant adverse effects and the discovery of new and more effective antifungal drugs [9-12].

Today, the triazoles, mainly Itraconazole and the allylamines, chiefly Terbinafine, are the main ammunition against dermatophytes. Unfortunately, in this era, treatment of Dermatophytosis, which was once very easy and uncomplicated for dermatologists, has become a nightmare. This is due to poor patient awareness, over-the- counter drugs, misuse of oral antifungals, combination topical medicines with steroids, and use of alternative treatment modalities. Hence, there is clinical resistance among patients with dermatophytosis [11-14].

Since it is the need of the hour to assess the therapeutic efficacy of the two most widely used oral antifungal drugs, Itraconazole and Terbinafine, hence this study is undertaken to compare the efficacy and safety of both the drugs.

2. MATERIALS AND METHODS

This is an open-label, randomized, a parallel study comparing Oral terbinafine and oral Itraconazolefor efficacy and safety in patients suffering from *Tineacruris* infections. This study was conducted in Sree Balaji Medical College and Hospital, Chennai during the period

from March 2016 to August 2016 by declaration of Helsinki and ICH -GCP guidelines. The Drug Therapy was given free of cost to the patients, till the end of the treatment period and they were instructed to bring the empty blister pack, to check for compliance. They were given assurance that any withdrawal from the study would not affect their future treatment in the same hospital.

The participants (study subjects) were selected based on the inclusion and exclusion criteria and were randomized with the help of a statistical software SPSS version 20 and allotted a treatment group. Each group had 50 patients. Baseline laboratory investigations were done before the onset of the study and participants received either one of the study drugs for 2 weeks (14 days). History was also obtained regarding diabetes milletus, hypertension and other co morbidities such as cardiac/ renal/ hepatic diseases, and medication history for these conditions if any was also noted.

There were four scheduled visits during the study; baseline visit, after 1st week, 2nd week (end of treatment visit) then 4th week (follow up for KOH scraping). All cases of dermatophytoses of the skin, diagnosed clinically were recorded along with age, sex, and duration of disease. Chronic and non-chronic cases were decided according to disease duration.

The patients who suffered from the disease for more than 6 months, with remissions and exacerbations, with orwithout a history of treatment, were taken as chronic cases.If the patient had been applying topical medication, it was stopped for at least 2 weeks and any antifungal systemic treatment was stopped at least 1 month before enrolling in the study.

Drug Dosage:

Group 1: Drug –Tab. Terbinafine: 11

Dose 500 mg per day once daily at bed-time for 2 weeks.

Group 2: Drug –Tab.traconazole:11

Dose 200 mg per day, once daily at bedtimefor 2 weeks.

The following Laboratory investigations were done during screening i.e. baseline visit (“0” weeks) and at the end of study i.e. 2 weeks. The Complete blood count, Random blood glucose (only at baseline visit).Repeated blood glucose for diabetics on follow up visits such as HbA1C for Diabetics (only at baseline visit), Serum urea and creatinine, Liver function test, Serum glutamic oxaloacetic transaminase (SGOT)and Serum glutamic pyruvic transaminase (SGPT).

2.1 Statistical Analysis

Data were entered into Microsoft excel datasheet and was analyzed using SPSS 20 version software. Categorical data was represented in the form of Frequencies and proportions.Chi square test was used as a test of significance for qualitative data and Independent t-test was used as test of significance to identify the mean difference between two quantitative variables and qualitative variables respectively.

3. RESULTS AND DISCUSSION

The patient attending dermatology OPD were screened and the study sample included 100 patients (as per the inclusion criteria) with dermatophyte infection of skin who attended outpatient departments. They were randomizedinto 2 groups for treatment – 1 (Terbinafine) and 2 (Itraconazole) and evaluated. p-value (Probability that the result is true)of <0.05 was considered as statistically significant after assuming all the rules of statistical tests. Following were the observations:

3.1 Comparison of Basic Demographic Statistics

The mean of subjects in the Terbinafine group was 39.2± 13.2 and in Itraconazole group was 27.3 ± 8.3 years. Majority of subjects in Group 1 were in the age group 31 to 40 years (30%), whereas the majority of subjects in Group 2 was in the age group 21 to 30 years.

Table 1. Age distribution comparison between two groups

Age of individuals	Group			
	Terbinafine count	%	Itraconazole count	%
<20 years	4	8.0%	11	22.0%
21 to 30 years	11	22.0%	24	48.0%
31 to 40 years	15	30.0%	12	24.0%
41 to 50 years	10	20.0%	3	6.0%
>50 years	10	20.0%	0	0.0%

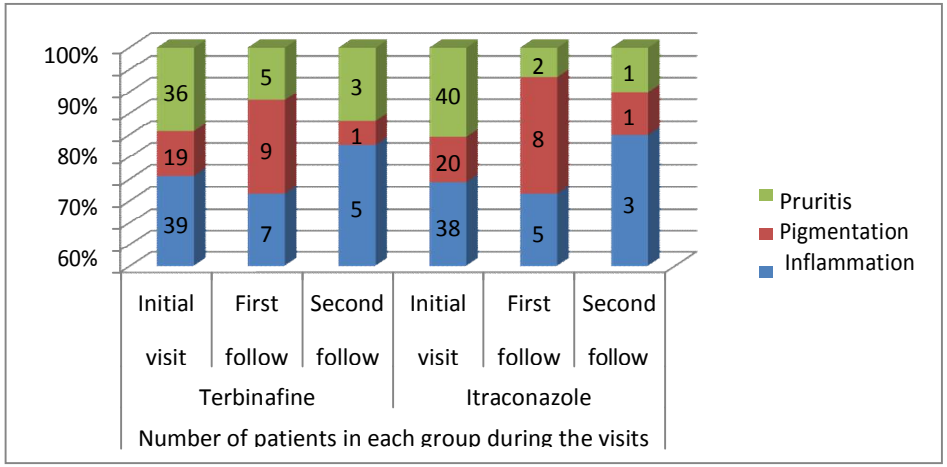

Fig. 2. Percentage distribution of Compositescore atinitial, first Follow up and after completion of treatment between two groups

Table 2. Gender distribution of subjects

Gender distribution	Group			
	Terbinafine		Itraconazole	
	Count	%	Count	%
Female	24	48.0%	17	34.0%
Male	26	52.0%	33	66.0%

Table 3. Composite scores in Group 1 and Group 2

	Group 1 n=50				Group 2 n=50			
	At baseline	At 1st week	At 2nd week	At 4th week	At baseline	At 1st week	At 2nd week	At 4th week
Mean ± SD	6.42±1.55	5.90±1.79	5.18±1.85	1.28±2.29	6.43±1.50	5.31 ± 1.92	3.21 ± 2.20	0.79± 1.76
Z value		4.10	5.08	6.03		5.16	5.51	5.58
P value		<0.05	<0.05	<0.05		<0.05	<0.05	<0.05

Majority of subjects in both the groups were males - 52% in group 1 and 66% in group 2 respectively. Females numbered 48% in group 1 and 34% in group 2.There was no difference in gender distribution between two groups.

3.2 Comparison of Baseline Composite Score between Two Groups

The participants distributedin both the groups have almost similar characteristics about their baseline compositescore.

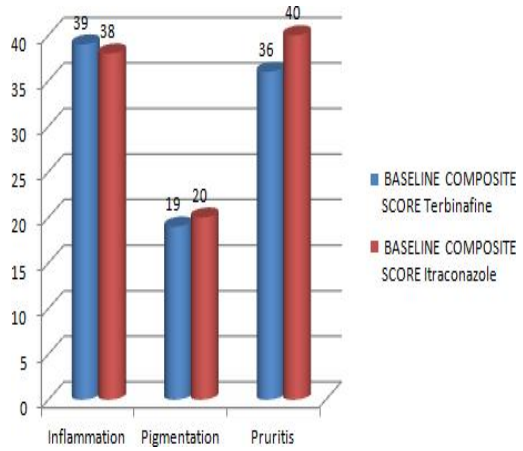

Fig. 1. Distribution of participants based on Baseline Composite score, Inflammation, pigmentation and pruritis between two groups (n=100)

There was a significant reduction in itching at the second follow-up (after 2 weeks of drug completion) in both groups. Pruritis was reduced in 92% of subjects in group 1 and 97.5% subjects in group 2.There was an 87% reduction in inflammation (erythema) in group 1 and a 93% reduction in group 2.Pigmentations were seen in 2% of subjects in both groups indicating relapse of the infection.

3.3 Comparison of Duration of Disease between Two Groups

In Group 1 duration of the disease was <6 months among 84% of subjects and 8% had >6 months duration.In Group 2, 86% of subjects had the disease for <6 months and 14% had the disease for >6 months.There was no significant difference in the duration of disease between the two groups.

Table 4. Duration of disease between two groups

Duration of disease	Number and percentage of patients in each Group			
	Terbinafine		Itraconazole	
< 6 Months	42	84.0%	43	86.0%
> 6 Months	8	16.0%	7	14.0%

3.4 Comparison of Previous Treatment History between the Two Groups

Table 5. Previous treatment history for tinea infection between two groups

Previous treatment history	Number and percentage of patients in each Group			
	Terbinafine		Itraconazole	
Steroids	23	46.0%	19	38.0%
None	13	26.0%	13	26.0%
Others	14	28.0%	18	36.0%

In Group 1, 46% had applied topical steroid or steroid combination with antifungal on their own (over-the-counter medications), 26% had not taken any treatment and 28% had either taken unknown systemic drugs/ applied oil or other natural remedies for the same condition. In Group 2, 38% had applied topical steroid or steroid combination with antifungal on their own (over-the-counter medications), 26% had not taken any treatment, and 36%% and had taken unknown systemic drugs/ applied oil or other natural remedies for the same condition.There was no significant difference in previous treatment between two groups.

3.5 Comparison of Comorbidities between the Two Groups

Table 6. Diabetic history comparison between two groups

Diabetes milletus	Number and percentage of patients in each group			
	Terbinafine		Itraconazole	
Yes	9	18.0%	8	16.0%
No	41	82.0%	42	84.0%

In Group 1, 18% of patients were diabetes milletusand in group 2, 16% had a history of diabetes. The majority of patients in both groups were non diabetics.There was no significant difference in diabetes history between two groups.

Table 7. Comparison of co-morbidities between two groups

Other co-morbidities	Number and percentage of patients in each group			
	Terbinafine		Itraconazole	
None	49	98.0%	49	98.0%
HTN	1	2.0%	0	0.0%
Other	0	0.0%	1	2.0%

In Group 1, 2% had Hypertension. In Group 2, 2% had other comorbidities – History of epilepsy. Majority of the patients did not have co-morbidities. There was no significant difference between two groups with respect to co morbidities.

Table 8. Examination–sites comparison between two groups

Examination–sites	Number and percentage of patients in each group			
	Terbinafine		Itraconazole	
TineaCruris	17	34.0%	18	36.0%
TineaCorporis	17	34.0%	16	32.0%
Multiple	16	32.0%	16	32.0%

In Group 1, 34% had T.*cruris*, 34% had T.*corporis* and 32% had multiple sites of infection.In Group 2, 36% had T.*cruris*, 32% had Tina corporis and 32% had multiple sites.There was no significant difference in examination sites between two groups.

Table 9. Scrapings comparison between twogroups at initial visit and final visit (aftertreatment)

KOH mount of fungal scrapings		Number and percentage of patients in each group				P-value
		Terbinafine		Itraconazole*		
Initial visit	Positive	50	100.0%	50	100.0%	-
After treatment	Positive	15	30.0%	6	12.0%	0.027*
	Negative	35	70.0%	44	88.0%	

At initial visit patients whose Scraping results were positive for fungal hyphae were only included in the study and hence it is 100% in both the groups indicating presence ofdermatophyte infection.

After treatment during final follow up visit: In KOH mount of the fungal scrapings,Group 1, 70 % were negative.88% were negative in Group 2 showing clearance of infection,this difference in post-treatment period with respect to clinical clearance was statistically significant for Itraconazole group.Group 2 (88%) that is Itraconazole group than in Group 1 (70%) Terbinafine group. P value was 0.027 which is statistically significant.

Table 10. % of diabetics who needed extension of treatment

Extension/change of drug	Number of patients and percentage in each group			
	Terbinafine Diabetic		Itraconazole Diabetic	
Extension ofdrug	9	81.8%	5	83.3%
Change ofdrug	1	9.1%	0	0.0%
P value	<0.001*		<0.001*	

Table 11. % of chronic cases that need extension

Groups	Duration of disease	Number and percentage of patients who need extension/change of drug				P-value
		Extension		Change		
Terbinafine	> 6 Months	7	53.8 %	1	100.0 %	<0.001*
Itraconazole	> 6 Months	3	50.0 %	0	0.0%	<0.001*

In Group 1/ Terbinafine group, 53.8% patients with chronic infection needed extension and 100% (1 patient) needed change of treatment.Similarly, in Group 2/ Itraconazole group, 50% patients with chronic infection needed extension of treatment.This observation was statistically significant.

4. DISCUSSION

Several RCTs support the efficacy of systemic antifungal drugs [12-17], Comparative trial between itraconazole 100 mg/day with ultramicronizedgriseofulvin 500 mg/day for tineacorporis or tineacruris showed significantly better clinical and mycological outcome in favor of itraconazole after 2 weeks of therapy [13]. A similar study comparing terbinafine with griseofulvin (both 500 mg daily for 6 weeks) for T.*corporis* found mycological cure rate of about 87% in the former group compared to 73% in latter14 A double-blinded study between itraconazole (100 mg/day) and griseofulvin (500 mg/day) found itraconazole to be superior in providing mycological cure [17]. There are not so many studies on comparison between Terbinafine and Itraconazole on250 mg/daywas administered for weeks [17]. However, recently, clinical failure and relapses have been observed withterbinafine in patients with tinea infections with increase in incidence ofterbinafine resistance [17]. Although resistance to terbinafinein dermatophytosis is not common in clinical practice, it has beenreported inclinical isolates by few authors [16]. Mukherjee et al. in 2003 reported the first confirmed report of terbinafine resistance in dermatophytes [16]. Majid et al. in their study 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. Authors concluded that incomplete mycological cure, as well as relapse was very common after standard (2 -week) terbinafine therapy in patients of tineacruris/corporis [18]. One of the principle mechanisms of antifungal drugs resistance is decrease in effective drug concentration [19], which in case of terbinafine is quite known feature following standard dosing regimen of 250 mg daily due to extensive accumulation in skin and adipose tissue [20].

This clearly shows that the current standard terbinafine therapy with 250 mg/day dose is not sufficient in current scenario where fungal resistance is further aggravated by increased use, inappropriate prescribing and, over the counter sale of antifungal drugs agents. [21,22] Even though there is no clear evidence as to what strategy should be used to best avoid resistance, 23the mostcommonly suggested measures in the past include prudent use of antifungal drugs and appropriate dosing with special emphasis on avoiding treatment with low anti-fungaldosage [22,23].

Similarly for Cutaneous fungal infections, R.J.Hay et al. [24] in their non-comparative studies using Itraconazole 100 mg/day demonstrate that 2 -week treatment courses generally produce clinical and mycological cure/marked improvement in />-80% of patients with dermatophyte infections affecting body areas, groin, and interdigital areas of the hand and foot; complete healing (clinical cure and negative mycology) may be observed in ≈ 50 to 80% of patients. Shorter higher itraconazole dosages (200 or 400 mg/day for a week) also produce similar cure rates, but a more rapid response is seen and are also beneficial in dermatomycoses [18-23]. Oral therapy is often chosen because of its shorter duration and the potential for greater patient compliance. Hence in our study we intended to compare the short maximum dosage regimen of the two widely used antifungal drugs and to identify the better antifungal drugs drug thanTerbinafine and Itraconazole in terms of clinical efficacy, safety profile and mycological clearance.

The study sample included 100 patients with dermatophyte infection of skin who attended outpatient departments. They were divided into 2 groups for treatment Group 1 received Tab. Terbinafine 500 mg/day for 2 weeks Group 2

received Itraconazole 200 mg/day for 2 weeks and evaluated.

4.1 Age and Sex Distribution

Majority of subjects in Group 1 were in the age group 31 to 40 years (30%), whereas majority of subjects in Group 2 were in the age group 21 to 30 years. The mean of subjects in Terbinafine group was 39.2 ± 13.2 and in Itraconazole group was 27.3 ± 8.3 years.This is in accordance with the age predilection of dermatophytoses. In a study by J. Decroix et al,1997, the mean age of tineacorporis/tineacruris patients was 39.7 years[18]. While Tineacruriscruris is found more frequently in children, Tineacruris and/or corporis is found most commonly in adults. In this study, males were found to be more commonly affected 52% in group 1 and 66% in group 2. Females numbered 48% in group 1 and 34% in group 2.

Earlier studies have also shown higher incidence of dermatophytosis in males 25-29. Skin surface lipids from female were observed to exert more potent fungistatic effect than males, this might be responsible for the lower incidence of infection in females 28.Males are more prone to tineacruris owing to the type of underwear, maceration and occlusion predisposing to growth of fungi . Females are more prone to tineacorporis due to occlusion caused by the saree at the waist [25].

The primary outcome of the study is as follows.

Composite score:

Table 12. Composite scores in GROUP 1 and GROUP 2

	At baseline		At 1st week		At 2nd week		At 4th week	
	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2
Mean ± SD	6.42 ± 1.55	6.43± 1.50	5.90 1.79	5.31 1.92	5.18 1.85	3.21 2.20	1.28 2.29	0.79 1.76
Z value	0.01		1.30		4.32		0.91	
P value	>0.05		>0.05		<0.05		<0.05	

In the present study the mean clinical score at baseline was Group 1(6.42 ± 1.55). 6.42 ± 1.52 and Group 2 (6.43 ±1.50). The maximum number of patients, i.e., 21 (22.82%) were in the score of 6. The minimum number of patients, i.e., 9 (9.78%) were in the score of 9 .There was significant decrease in the clinical score beginning from baseline to 4th week in both the groups (P< 0.05). After 4 week of therapy the maximum number of patients, i.e., 79% were in the score of zero (Group 1 - 35patients, i.e.,70% and Group 2 -44 patients, i.e., 88%).

Effectiveness of the treatment was assessed by the global clinical evaluation criteria, the clinical findings are rated as:

Healed (absence of signs and symptoms),
Markedly improved (>50% clinical improvement),
Considerable residual lesions (<50% clinical improvement),
No change, E. Worse

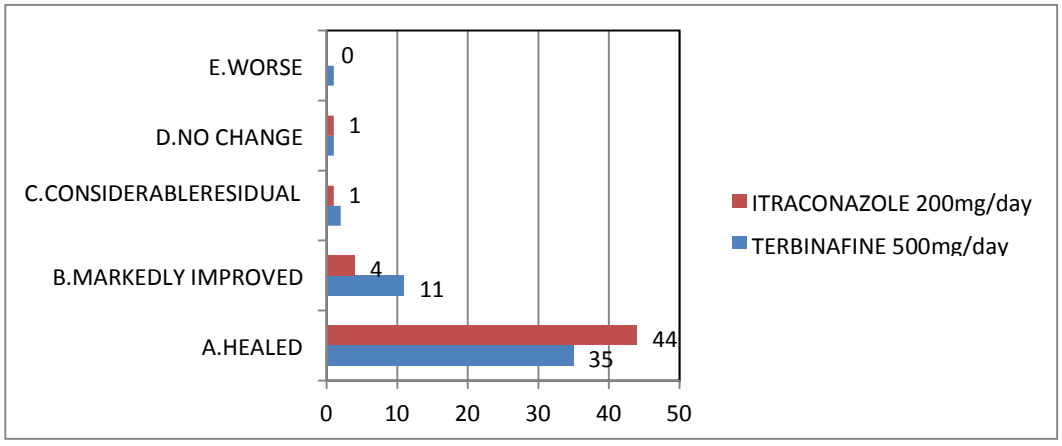

Fig. 3. Clinical cure rates for group 1 vs group 2

This was confirmed by KOH mount of scrapings which showed that new lesions were seen in 1 patient- 2% of group 1 and none in group 2.Mycological cure was better in group 2 (88%) compared to group 1 (70%).30% patients in group 1 showed less clearance of lesions compared to 12% in group 2.Thus, significant difference was observed between two groups with respect to clinical clearance and was found to be statistically significant.. A study was done to determine the MIC values of terbinafine and itraconazole against the common dermatophyte speciesTrichophytonrubrum and T. mentagrophytes. It was found that – Itraconazole had lower mean MIC value as compared to terbinafine, suggesting that it might be more effective. Trichophytonmentagrophyte isolates were found more susceptible to itraconazole as compared to terbinafine since lower MIC50 value of 0.125 µg/ml was seen against 0.5 µg/ml for terbinafine. Similar results were seen for T. rubrum [26].

The MIC50 and MIC90 values of terbinafine were recorded at 0.5 µg/ml and 2 µg/ml respectively. This was higher than itraconazole.Even though this study was not on species determination, Group 2 responded better might be of this reason.

The secondary outcome of the study is as follows.

Post-treatment LFT:

Table 13. Post treatment LFT comparison between two groups

Post treatment LFT	Number and percentage of patients in each Group			
	Terbinafine		Itraconazole	
Normal	47	94.0%	49	98.0%
Abnormal	3	6.0%	1	2.0%

In Group 1, 6% had an abnormal LFT.

In Group 2, 2% developed abnormal LFT after treatment.

Both results showed a transient raise in liver enzymes which returned to normal within 4 weeks of completion of treatment. This was not clinically significant.

Post treatment LFT was assessed in all patients and it was found that 3 patientsin Group 1/ Terbinafinegroup and1 patient in Group 2/ Itraconazole group had mildly elevated liver enzymes. These patients did not have history of liver disease/ did not take any medication that was hepatotoxic. The elevated levels returned to normal within4 weeks of completion of treatment. Hence it was not significant.Both terbinafine30 and Itraconazole31 have propensity to cause hepatotoxicity but it is very rare. These patients did not have any clinical symptoms or features of liverinjury; therefore, the rise in enzymes was mild and transient.

Adverse events:

Table 14. Adverse events comparison between two groups

Adverse Events	Number and percentage of patients in each Group			
	Terbinafine		Itraconazole	
Headache	14	28.0 %	13	26.0 %
GI Symptoms	14	28.0 %	7	14.0 %
None	22	44.0 %	30	60.0 %

In Group 1, 28% developed headache, 28% developed GI symptoms and 44% had no adverse effects.In Group 2, 26% developed headache, 14% developed GI symptoms and 60% had no adverse effect. This was not clinically significant .There was no discontinuation of treatment due to adverse effects. There was no significant difference in adverse event between two groups.

The host factors for chronicity include - diabetes mellitus, atopy, and intake of systemic corticosteroids, keratinization disorders, hypercorticolism and poor personal hygiene. This is in accordance with Jolly HW et al., in his study he found correlation between Oral glucose tolerance abnormality and recurrent Trichophytonrubrum infections. In this study it was evident diabetes had contributed for extension of therapy. Diabetes has often been associated with dermatophytoses of skin and onychomycosis.In our study, 18 % in the terbinafine group and 16% in the Itraconazole group had diabetes. Studies have shown correlation between diabetic duration, poor glycemic control and dermatophytosis [27,28] interestingly, out of 100 subjects in our study 17 were diabetic patients and 52.9% had chronic infection and similarly, out of 15 subjects with

chronic infection, 60% were diabetics. This is an important finding which shows direct relationship between diabetes and chronicity of dermatophytosis [27], which should be kept in mind and treated optimally.

The pharmacological factors could be over the counter (OTC) medications, self-medication like misuse of steroid [22,23,26,29,30-33] or steroid combination with antifungal drugs preparation187for faster relief of symptoms. Precise bioavailability studies were also essential. Previous treatment was prevalent among the study subjects, with almost 40% in each group having used a topical steroid combination. 30 -40% of subjects had also taken unknown systemic treatment with or without antifungal drugs, natural remedies like oil application etc.This reflects the poor awareness and delay in seeking appropriate treatment. The patients must be counselled against these practices. Topical steroids could alter the course of disease by suppressing inflammation and giving a sense of relief, only for the infection to relapse once its use is stopped. Coondoo A et al., in his study on side effets of topical steroid, he described that the p rolonged steroid use can also lead to striae, atrophy, telangiectasia and ulceration of skin and increase susceptibility to other infections [26].

4.2 Co-morbidities and Other Treatments

The comorbidities of patients were investigated. Terbinafine and Itraconazole are both contra indicated in Chronic/ active liver disease/ concomitant use of other hepatotoxic drugs and in poor renal function. Itraconazole is also contra-indicated in congestive heart failure, must not be given with drugs such as terfenadine, astemizole, quinidine, ergot alkaloids, midazolam, triazolam and can alter the levels of many other drugs.In order to avoid these potential adverse effects and interactions, caution was taken to obtain detailed history from the patients. If the patient had been on any other treatment which could interact with the drugs being studied, it must be discontinued (if possible) for at least one month prior to starting antifungal drugs treatment. These conditions are explained in the exclusion criteria.

5. CONCLUSION

The increasing burden of chronic dermatophytosisis felt all across the country. What is seen in the outpatient departments is only the tip of the iceberg. The vast numbers of hidden and undiagnosed cases remains and poses a significant threat to the community. These patients act as reservoirs and re-infect their surroundings and contribute to communal infection and possibly an epidemic. Clinical resistance, which is often more complex and caused by a number of reasons but treatment extension is mainly due to host factors, agent factors and pharmacological factors.Antifungal drugs such as Itraconazoleand terbinafinestill hold their ground in effective treatment of dermatophytosis. Creating awareness about the contributing factors, good patient counselling, adequate and judicious use of antifungal drugs both in correct dose and duration are keys in controlling the rapid increase in chronic and resistantdermatophytoses.

CONSENT AND ETHICAL APPROVAL

The study protocol was reviewed and approved by the Institutional Ethics Committee and all trial participants have been informed about the study procedures and written informed consent was obtained.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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