e-ISSN: 0976-822X, p-ISSN:2861-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2023; 15(7); 123-128

Original Research Article

A Randomized Comparative Assessment of the Efficacy of Terbinafine and Itraconazole in Increased Dosages and Duration in the Treatment of Tinea Corporis and Tinea Cruris

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Received: 10-4-2023 Revised: 20-05-2023 / Accepted: 25-06-2023
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Conflict of interest: Nil

Abstract

Aim: This study was designed to compare the efficacy of terbinafine and itraconazole in increased dosages and duration in the treatment of tinea corporis and tinea cruris.

Material & methods: In this randomized comparative study carried out at Department of Pharmacology, DMCH, Laheriasarai, Darbhanga, Bihar, India for 11 months, patients of tinea cruris and tinea corporis were randomly divided into two groups of 100 each and were given oral terbinafine (Group I) and oral itraconazole (Group II) for 4 weeks. The scores and percentage change in scores of pruritus, scaling, and erythema were evaluated at 2 and 4 weeks.

Results: The mean age of patients was 32.48±12.18 and 31.29±11.15 years respectively, in group A and group B. Group A had 35 (70%) males and 15 (30%) females, while in group B there were 34 (68%) males and 16 (32%) females. Tinea corporis et cruris (40 patients in group A and 34 patients in group B) was most common type of dermatophytic infection followed by tinea cruris (6 patients in group A and 10 patients in group B) and tinea corporis (4 patients in group A and 6 patients in group B). Statistically, there was no significant difference between two groups for symptom scores for all the three symptoms at baseline. Improvement in all the three symptoms (erythema, scaling and pruritus) was seen from the first follow-up at 2 weeks itself.

Conclusion: Itraconazole has shown a higher mycological and clinical cure rate when compared to Terbinafine. Patients who were prescribed Terbinafine have indicated that there is a growing resistance to the drug and increased chances of failure of treatment of dermatophytic infections, failure of therapy also add to the financial burden on patients.

Keywords: Efficacy, Itraconazole, Terbinafine, Tinea Corporis, Tinea Cruris

Introduction

Dermatophytes are group of filamentous fungi that require keratin for growth. The condition produced as a result of dermatophyte infection is commonly known as dermatophytosis. The dermatophyte infections can cause cutaneous changes in the skin by forming ring shape lesions with a clear center and inflammatory edge and owing to this they are often also termed as ringworm. [1,2]]

Tinea is a superficial fungal infection caused by dermatophytes which invade and multiply within the keratinized tissue (skin, hair, nails). Approximately 20%-25% of the world population is affected by tinea. [3] There is a rise in the prevalence in recent years especially in the tropical countries [4] along with an increase in the number of chronic and recurrent dermatophytosis. Over the past few years, it has been observed and recorded that dermatophyte infections have increased by many times in India. There is a remarked change in the disease presentation, severity, treatment response, and relapse rate. However, the causes may even be more diverse, from the irrational use of antifungal drugs to topical steroid usage and to the poor socioeconomic status of the population. [5]

Antifungal agent and antimycotic are unremarkably used oral antifungal agents for the same. However, resistance to those medication is being seen progressively once utilized in the standard doses and length. [6] Terbinafine is a fungicidal drug and acts by inhibiting the enzyme squalene epoxidase which converts squalene to lanosterol due to its activity against the fungal infections and pharmacokinetic profile. Mechanism of action is by inhibiting the enzyme squalene oxidase, thereby inhibiting ergosterol synthesis. [7] There has been an increase in resistance in the incidence of terbinafine recently with increasing numbers of clinical failures and relapses. [8,9]

Antifungal resistance is due to decrease in effective drug concentration. Terbinafine at higher doses of 500mg/day was reported to be efficacious and safe. Itraconazole is a triazole class of broad-spectrum antifungal that that acts through inhibition of the enzyme 14α-demethylase. [10] It acts by slowing down the growth of fungi through inhibition of ergosterol synthesis that helps to maintain the cell membrane in the fungi. [11] It has been found to be highly effective against dermatophytes, candida, and on some non dermatophytic molds. [12] Side effects includes most commonly gastrointestinal upset where as others are rashes/pruritus, hypokalemia, headache, hypotension, leukocytopenia as well as renal impairment. [13] It acts by inhibiting cytochrome P450-dependent enzyme, hence interfering with demethylation of lanosterol to ergosterol. When given at a dose of 100mg once a day for 2 weeks and with 200mg once a day for 7 days it has shown good results and efficient in managing the dermatophytosis.

Hence, the present study was planned to compare the clinical efficacy of oral itraconazole (100 mg BD) and terbinafine (250 mg BD) in treatment of dermatophytic infection of skin.

Material & Methods

A prospective, randomized and comparative study carried out at Department of Pharmacology, DMCH, Laheriasarai, Darbhanga, Bihar, India. The duration of the study was of 11 months. Sample size was 100 patients.

Inclusion criteria

- Freshly diagnosed patients of aged 18 years and above with clinical diagnosis of tinea corporis and tinea cruris confirmed by potassium hydroxide (KOH) test attending Department of Pharmacology, DMCH, included in study.

Exclusion criteria

- Previously treated patients, patients with pre-existing renal disease hepatic disease and cardiac disease and pregnant and lactating women were excluded.

The patients were randomly allocated to receive a daily dose of terbinafine 500 mg daily for 4 weeks (Group I) or 200 mg of itraconazole for 4 weeks daily (Group II). The study was approved by the Institutional Ethics Committee, and

informed consent was taken from all patients before recruiting.

Mycological and clinical assessments

Patients were followed up after 2 weeks and 4 weeks of the study period. At each visit, clinical response was noted including pruritus, erythema, and scaling. These were rated as clinical score 0–3, 0 – absent, 1 – mild, 2 – moderate, and 3 – severe.

Global clinical evaluation was done, and the response was noted accordingly as healed, marked improvement, considerable residual lesions (>50%), no change, or worse. KOH examination was done at the time of enrolling the patient and at the end of the 4th week. Liver function tests were done at the start of therapy and after 2 weeks of therapy. Monitoring of signs and symptoms for any adverse cardiac event was done at each visit, especially for high-risk patients (diabetics and hypertensives) on itraconazole. Patients were considered cured when there was an absence of scaling, erythema, and pruritus, and KOH was also negative. Post-inflammatory pigmentary changes were not taken into consideration.

Statistical Analysis

Association among dichotomous variables was tested with Fisher's exact test and continuous variables with a student's test. Percentage change was compared using Mann–Whitney U-test and Wilcoxon test. All analysis was done SPSS version 21.0 (IBM Corp., Armonk, NY)

Results

Table 1: Demographic profile and diagnosis of patient

Characteristic	Group A, (n=50)	Group B, (n=50)	P value
Mean age±SD (range) (years)	32.48±12.18 (18-64)	31.29±11.15 (18-61)	p=0.675
Sex			
Male	35 (70)	34 (68)	p=0.630
Female	15 (30)	16 (32)	
Diagnosis			
Tinea corporis	4 (8)	6 (12)	
Tinea cruris	6 (12)	10 (20)	p=0.080
Tinea corporis and cruris	40 (80)	34 (68)	
Occupation			
Unskilled worker/ farmer	10 (20)	10 (20)	
Skilled worker/ vendor	8 (16)	10 (20)	
Clerk/ shopkeeper/ teacher	8 (16)	6 (12)	p=0.720
Officer/ professional	2 (1)	8 (4)	
Homemaker	9 (18)	6 (12)	
Student	13 (26)	10 (20)	

The mean age of patients was 32.48±12.18 and 31.29±11.15 years respectively, in group A and group B. Group A had 35 (70%) males and 15 (30%) females, while in group B there were 34 (68%) males and 16 (32%) females. Tinea corporis et cruris (40 patients in group A and 34 patients in group B) was most common type of dermatophytic infection followed by tinea cruris (6 patients in group A and 10 patients in group B) and tinea corporis (4 patients in group A and 6 patients in group B). Majority of the patients in both group were students and homemaker followed by farmers.

Table 2: Clinical parameters in Group A (Itraconazole) and B (Terbinafine)

Characteristics	Group A, (n=50) (%)				Group B, (n=50) (%)				'p' value
	No	Mild	Mod	Severe	No	Mild	Mod	Severe	
At enrolment (Baseline)									
Erythema	0	1 (2)	14 (28)	35 (70)	0	0	20 (40)	30 (60)	p=0.171
Scaling	0	8 (16)	39 (78)	3 (6)	0	6 (12)	37 (74)	6 (12)	p=0.325
Pruritus	0	2 (4)	48 (96)	0	0	1 (2)	49 (98)	0	p=0.620
First follow-up	n=50					n=50			
Erythema	2 (1)	14 (28)	34 (68)	2 (4)	2 (1)	13 (26)	32 (64)	4 (8)	p=0.715
Scaling	8 (16)	36 (72)	5 (10)	0	4 (8)	35 (70)	10 (20)	0	p=0.060
Pruritus	0	4 (8)	40 (80)	5 (10)	2 (4)	42 (84)	5 (10)	0	p=0.420
Second follow-up	n=47				n=48				
Erythema	15 (25.5)	34 (72.34)	4 (8.51)	0	10 (20.83)	30 (62.5)	10 (20.83)	0	p=0.210
Scaling	40 (85.1)	88 (17.02)	1 (2.12)	0	30 (62.5)	20 (41.66)	0	0	p=0.002
Pruritus	8 (17.02)	24 (51.06)	15 (31.91)	0	1 (2.08)	29 (60.41)	16 (33.34)	0	p=0.044
Third follow-up	n=46				n=47				
Erythema	35 (76.08)	10 (21.73)	0	0	30 (63.82)	15 (31.91)	0	0	p=0.320
Scaling	44 (95.65)	3 (4.34)	0	0	40 (85.10)	7 (14.89)	0	0	p=0.044
Pruritus	34 (73.91)	7 (15.21)	2 (4.34)	0	30 (63.82)	12 (25.53)	3 (6.38)	0	p=0.180

Statistically, there was no significant difference between two groups for symptom scores for all the three symptoms at baseline. Improvement in all the three symptoms (erythema, scaling and pruritus) was seen from the first follow-up at 2 weeks itself.

Discussion

The most common fungal infections are the dermatophytic infections affecting 20 - 25% population globally. In India, hot and humid climate favours dermatophytosis. Over the past few years, it has been observed and recorded that dermatophyte infections have increased by many times in India. There is a remarked change in the disease presentation, severity, treatment response, and relapse rate. However, the causes may even be more diverse, from the irrational use of antifungal drugs to topical steroid usage and to the poor socioeconomic status of the population. [14] Antifungal agent and antimycotic are unremarkably used oral antifungal agents for the same. However, resistance to those medication is being seen progressively once utilized in the standard doses and length. [15] The first line of drug for the treatment of dermatophytic infections is Terbinafine due to its activity against the fungal infections and pharmacokinetic profile. Mechanism of action is by inhibiting the enzyme squalene oxidase, thereby inhibiting ergosterol synthesis. [16]

The mean age of patients was 32.48±12.18 and 31.29±11.15 years respectively, in group A and group B. Group A had 35 (70%) males and 15 (30%) females, while in group B there were 34 (68%) males and 16 (32%) females. Tinea corporis et cruris (40 patients in group A and 34 patients in group B) was most common type of dermatophytic infection followed by tinea cruris (6 patients in group A and 10 patients in group B) and tinea corporis (4 patients in group A and 6 patients in group B). Statistically, there was no significant difference between two groups for symptom scores for all the three symptoms at baseline. Improvement in all the three symptoms (erythema, scaling and pruritus) was seen from the first follow-up at 2 weeks itself. Itraconazole is generally well tolerated. However, certain side effects have been reported with its use. Most commonly encountered side effects were Gastrointestinal upset followed by rashes/ pruritus, headache, hypotension in small number of patients. [7] Terbinafine resistance when given in the standard doses (250 mg OD for 2 weeks) is increasingly leading to partial or no response for treatment of dermatophytic infection.17 Hence, higher dosage regimen for longer duration has been found to be more effective. The most common adverse events associated with terbinafine tend to be mild and self-limited. These include headaches, gastrointestinal symptoms, and rash. [18]

Dermatophytic infections of skin are caused by a group of fungi that affect the superficial layer of skin. Antifungals are the mainstay of medical management of dermtophytes both in topical as well as oral form. Triazoles-particularly Itraconazole is one of the most commonly used antifungals that has been reported to be highly effective against dermatophytes. [12] The findings of the present study, thus show a slightly better efficacy of itraconazole over terbinafine in terms of symptom resolution, however, the two drugs were comparable in terms of overall response rate. The findings of the present study must be viewed in specific context of drug-dose combination and duration of treatment. Further studies on variable drug-dose combinations and duration of treatment are recommended to settle the issue of optimum dosing, drug selection and duration of treatment and a sufficient post-treatment follow-up to evaluate the efficacy of two drugs to study their efficacy in terms of recurrence prevention.

Conclusion

Itraconazole has shown a higher mycological and clinical cure rate when compared to Terbinafine. Patients who were prescribed Terbinafine have indicated that there is a growing resistance to the drug and increased chances of failure of treatment of dermatophytic infections, failure of therapy also add to the financial burden on patients. The findings of the study showed that for a 6-week regimen, both itraconazole and terbinafine offered similar response. Though statistically non-significant yet a proportional response to treatment was better in itraconazole as compared to terbinafine. Further studies with larger sample size could determine the statistical significance of these differences in a better way.

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