Section: Pharmacology

Original Research Article

COMPARATIVE ANALYSIS OF ORAL TERBINAFINE VERSUS ITRACONAZOLE IN TREATMENT OF DERMATOPHYTIC INFECTIONS

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Received : 07/03/2024
Received in revised form : 20/03/2024
Accepted : 11/04/2024

Keywords:
Terbinafine, Itraconazole, Dermatophytic.

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DOI: 10.47009/jamp.2024.6.2.172

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (2); 832-835

Abstract

Background: The dermatophytes' ability to attach to the keratinized tissue of skin forms the basis for the dermatophytosis. Oral terbinafine has been demonstrated to be the most effective treatment for the mycological cure of toenail dermatophyte infections. Itraconazole can treat many different fungal infections. Hence, the present study was conducted for assessing the efficacy of oral terbinafine versus itraconazole in treatment of dermatophytic infection of skin. **Materials and Methods:** A total of 80 patients were enrolled. Complete demographic and clinical details of all the patients were obtained. All the patients were divided into two study groups as follows: Group 1: Oral terbinafine group (tablet terbinafine 250 mg twice daily) and Group 2: Itraconazole (Itraconazole 100 mg tablet twice daily) group. Clinical diagnosis of tinea corporis and tinea cruris was confirmed by potassium hydroxide (KOH) test. Follow-up evaluation was done and at each follow up visit clinical responses were observed clinically scored as 0-3 in which 0-absent, 1-mild, 2-moderate, 3-severe. All the results were obtained and subjected to statistical analysis using SPSS software. **Result:** A total of 80 patients were enrolled and divided into two study groups with 40 patients in each group. The mean age of the patients of group A and group B was 45.3 years and 41.7 years respectively. Majority proportion of patients of both the study groups were males. While comparing the scaling and erythema at different follow-up time intervals, significant results were obtained. **Conclusion:** Our results demonstrated that Itraconazole has better results in comparison to terbinafine. So itraconazole is superior to terbinafine in treatment of dermatophytic infection of skin.

INTRODUCTION

The dermatophyte's ability to attach to the keratinized tissue of skin forms the basis for the dermatophytoses (superficial fungal skin infections). They are superficial fungal infections caused by dermatophytes affecting the skin, hair and/or nails. They are also termed tinea infections. Dermatophytes are filamentous fungi that invade and feed on keratinized tissue like skin, hair and nails, causing an infection. Dermatophytes are divided into nine genera, of which Trichophyton (usually affecting skin, hair and nails), Epidermophyton (usually affecting skin) and Microsporum (usually affecting skin and hair) cause infection in humans. *Trichophyton rubrum* is the most common isolate observed in infections of the feet, body and nails.[1- 3]

General measures like loose-fitting cotton or synthetic clothing which wick moisture away from skin surface are advisable. In addition, patients should be discouraged from sharing garments and towels. Undergarments, socks, and caps should be regularly washed and dried in the sun and ironed. Patients with tinea cruris may be assessed for associated conditions that may contribute to occlusion and thus persistence/recurrence viz. excessive sweating or obesity. Here, encouraging patients to change clothing more frequently, use absorbent powders and deodorants (decrease perspiration), and lose weight, if required, may be advisable.[4,5] Oral terbinafine has been demonstrated to be the most effective treatment for the mycological cure of toenail dermatophyte infections. Treatment of onychomycosis in the pediatric population with systemic medications is off-label, and it is not U.S.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Food and Drug Administration (FDA) approved. Although there are no proposed USA guidelines, terbinafine has been recommended by the British Association of Dermatologists as a first-line treatment. Most antifungal medications work through the inhibition of fungal membrane production and ergosterol synthesis. Terbinafine is an allylamine that works early in the pathway as a non-competitive inhibitor of the enzyme squalene epoxidase and subsequent conversion of squalene-to-squalene epoxide. Although not directly fungicidal, the intracellular accumulation of squalene results in fungal cell death.[6-8]

Itraconazole can treat many different fungal infections. Many of these fungal infections are rare; however, they can be detrimental to the immunocompromised. Itraconazole (sometimes abbreviated ITZ) treats blastomycosis, histoplasmosis, and aspergillosis and has FDA approval as a treatment for these infections. However, itraconazole has also shown efficacy in treating paracoccidioidomycosis, coccidioidomycosis, and candidiasis, but it does not have FDA approval for these conditions. In addition to treating infections, itraconazole can be used as prophylaxis in patients at risk of these systemic fungal infections.[9,10] Hence, the present study was conducted for assessing the efficacy of oral terbinafine versus itraconazole in treatment of dermatophytic infection of skin.

MATERIALS AND METHODS

The present study was conducted in the Department of Pharmacology, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh (India) for assessing the efficacy of oral terbinafine versus itraconazole in treatment of dermatophytic infection of skin for 1 year. A total of 80 patients were enrolled. Present study was conducted after approval from institutional ethics committee. Complete demographic and clinical details of all the patients were obtained. Inclusion criteria for the present study included patients with dermatophytic infection. All the patients were divided into two study groups as follows:

Group 1: Oral terbinafine group (tablet terbinafine 250 mg twice daily) and

Group 2: Itraconazole (Itraconazole 100 mg tablet twice daily) group

Clinical diagnosis of tinea corporis and tinea cruris was confirmed by potassium hydroxide (10% KOH) test. Follow-up evaluation was done and at each follow up visit clinical responses were observed clinically scored as 0-3 in which 0-absent, 1-mild, 2-moderate, 3-severe. All the results were obtained and subjected to statistical analysis using SPSS software version 21.

RESULTS

A total of 80 patients were enrolled and divided into two study groups with 40 patients in each group. The mean age of the patients of group A and group B was 45.3 years and 41.7 years respectively. Majority proportion of patients of both the study groups were males in which male female ratio found 3:1. While comparing the scaling and erythema at different follow-up time intervals, significant results were obtained.

Table 1: Comparison of scaling at different time intervals

Scaling		Group A	Group B	p-value
Baseline	No	0	0	0.112
	Mild	6	8	
	Moderate	6	10	
	Severe	28	22	
Fist follow-up	No	0	0	0.638
	Mild	10	14	
	Moderate	12	14	
	Severe	18	12	
Second follow-up	No	0	0	0.000 (Significant)
	Mild	14	18	
	Moderate	10	16	
	Severe	10	6	

Table 2: Comparison of erythema at different time intervals

Erythema		Group A	Group B	p-value
Baseline	No	0	0	0.651
	Mild	8	10	
	Moderate	10	10	
	Severe	22	20	
Fist follow-up (2 weeks)	No	0	0	0.249
	Mild	10	12	
	Moderate	14	12	
	Severe	16	16	
Second follow-up (6 weeks)	No	0	2	0.001 (Significant)
	Mild	14	18	
	Moderate	14	14	
	Severe	12	4	

ISSN (O): 2687-5365; ISSN (P): 2753-6556

DISCUSSION

Superficial fungal infections account for nearly 25% of the global skin mycoses, making dermatophytic infections one of the most common types of infective diseases worldwide. Dermatophytosis refers to a superficial mycotic infection caused by either of the three groups of keratinophilic fungi, namely, Trichophyton (infects skin, nails, hair), Microsporum (skin and hair), and Epidermophyton (skin and nails). These comprise the most common agents responsible for superficial cutaneous fungal infections.[11,12] Successful management of dermatophytosis has increasingly become challenging owing to the changing epidemiological factors and the emergence of drug resistant organisms. Appropriate dose and duration of drug in a compliant patient helps achieve successful mycological cure. In addition to pharmacological therapy, general measures and lifestyle changes also play a crucial role in preventing recurrences. Improved diagnostic tests and novel immunomodulatory therapy portend advances in disease management.[13,14]

Itraconazole is an orally active triazole antifungal drug which has demonstrated a broad spectrum of activity and a favourable pharmacokinetic profile. It is a potent inhibitor of most human fungal pathogens including *Aspergillus* sp. In non-comparative clinical trials itraconazole was shown to be extremely effective in a wide range of superficial and more serious 'deep' fungal infections when administered once or twice daily. Generally, greater than 80% of patients with superficial dermatophytic or yeast infections are cured by itraconazole. Similarly, good to excellent response rates (clinical cure or marked improvement) are achieved in paracoccidioidomycosis, histoplasmosis, sporotrichosis, blastomycosis, systemic candidiasis, coccidioidomycosis, chromomycosis, aspergillosis and cryptococcosis.[15]

FDA-approved oral treatment for onychomycosis includes terbinafine and itraconazole, and fluconazole are used off-label. Due to fewer collateral effects and higher cure rates, terbinafine is usually preferred over itraconazole. The standard dosage is 250 mg per day for 6 weeks for fingernails or 12 weeks for toenails. Some pharmacokinetic studies have shown that terbinafine can be detected in the nail plate in concentrations above the minimal inhibitory concentrations for dermatophytes and other fungi 36 weeks post-treatment. Pulse regimens have been proposed to reduce the side effects and risks of interaction with other medication. Most studies have shown a superior efficacy of terbinafine compared to itraconazole pulse regimens and similar efficacy compared to a conventional terbinafine dose.[16,17]

Hence, the present study was conducted for assessing the efficacy of oral terbinafine versus itraconazole in treatment of dermatophytic infection of skin.

A total of 80 patients were enrolled and divided into two study groups with 40 patients in each group. Mean age of the patients of group A and group B was 45.3 years and 41.7 years respectively. Majority proportion of patients of both the study groups were males. While comparing the scaling and erythema at different follow-up time intervals, significant results were obtained. Bhatia A et. al., compared the efficacy of terbinafine and itraconazole in increased dosages and duration in the treatment of tinea corporis and tinea cruris. Patients of tinea cruris and tinea corporis were randomly divided into two groups of 160 each and were given oral terbinafine (Group I) and oral itraconazole (Group II) for 4 weeks. At the end of week 4, mycological cure was seen in 91.8% after 4 weeks in the itraconazole group as compared to 74.3% of patients in the terbinafine group. There was a significant improvement in percentage change in pruritus, scaling, and erythema in both the groups from 0 to 4 weeks. On comparing groups, the percentage change was significantly different in scaling from 0 to 2 weeks and 2-4 weeks between Group I and Group II, respectively. Clinical global improvement was better with itraconazole. Mild adverse effects such as gastrointestinal upset, headache, and taste disturbances were observed which were comparable in both the groups. Itraconazole and terbinafine seem to be equally effective and safe in the treatment of tinea cruris and tinea corporis.[18]

Hassaan et. al., compared the efficacy of either terbinafine or itraconazole orally versus the combination of the two drugs in the treatment of recalcitrant dermatophytosis. It included 45 patients with recalcitrant dermatophytosis who were distributed into 3 groups (each of 15 patients); Group A received terbinafine 250 mg twice a day for 4 weeks. Group B received itraconazole 200 mg twice a day for 4 weeks. Group C received terbinafine 250 mg once daily and itraconazole 200 mg once daily for 4 weeks. At the end of twelve weeks, 12 (80%) patients in group A; 13 (86.7%) patients in group B and 15 (100%) patients in group C were completely cured. Despite cure rates being higher in the combined group C; yet results were not statistically significant. Clinical cure rates were not significantly higher in itraconazole + terbinafine combined group.[19]

Kumar G et. al., in another study, assessed the efficacies of two antifungal drugs with their increased dosages and duration. 145 Patients were randomized into two groups A and B. Group A patients were given capsule itraconazole 100 mg twice daily and group B were given tablet terbinafine 250 mg twice daily, both for 6 weeks. Patients were followed up at 2, 4 and 6 weeks and at each visit, scores for 3 parameters (erythema, scaling and pruritus) were recorded and analysed. A total of 140 patients completed the study with 72 patients in group A and 73 patients in group B. In group A 72.5% of patients achieved complete remission compared to 67.6% in group B. At each follow up patients were evaluated

ISSN (O): 2687-5365; ISSN (P): 2753-6556

based on total symptom score (erythema, scaling and pruritus) which had shown significant improvement with negative potassium hydroxide results. None of the patients had severe side effects. Study showed that Itraconazole has higher clinical and mycological cure rates as compared to terbinafine.[20]

CONCLUSION

Our results demonstrated that Itraconazole has better results in comparison to terbinafine. So itraconazole is superior to terbinafine in treatment of dermatophytic infection of skin.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556