

Original Article

Efficacy of Oral Voriconazole versus Terbinafine in Patients with Recalcitrant Tinea Cruris: A Single-Center Prospective Study from Peshawar

Murad Ali*, Sahibzada Mehmood Noor, Samreen Javed, Bashir Ahmad, Sabahat

Department of Dermatology, Lady Reading Hospital, Peshawar.

Abstract

Background Recalcitrant tinea cruris has emerged as a major therapeutic challenge due to increasing antifungal resistance and insufficient response to conventional therapy (terbinafine, clotrimazole, miconazole and ketoconazole creams). Terbinafine and voriconazole are commonly considered in resistant cases; however, their comparative effectiveness remains uncertain.

Objective To compare the efficacy of voriconazole versus terbinafine in the treatment of recalcitrant tinea cruris.

Methods This comparative prospective cohort study included 300 patients aged 20 to 70 years with recalcitrant tinea cruris who failed to respond to one month of topical antifungal therapy were included in the study. Patients were assigned equally into two groups. Group A received oral voriconazole 400 mg once daily, while Group B received oral terbinafine 250 mg twice daily for four weeks. Treatment efficacy was assessed at eight weeks post-treatment. Data were analyzed using SPSS version 25. The chi-square test was used to compare efficacy with significance set at $p \leq 0.05$.

Results The voriconazole group achieved a significantly higher complete resolution rate of 81.3% (n=122) compared to 63.3% (n=95) in the terbinafine group ($P < .001$). Partial resolution was observed in 14.0% (n=21) patients in the voriconazole group and 24.0% (n=36) in the terbinafine group. No change was observed in 4.7% (n=7) cases in the voriconazole group and 12.7% (n=19) in the terbinafine group. Adverse events were comparable between groups ($P = .161$).

Conclusion Voriconazole exhibited superior efficacy compared to terbinafine in achieving complete resolution of recalcitrant tinea cruris at eight weeks post-treatment, with an acceptable safety profile.

Keywords Antifungal agents; Efficacy; Terbinafine; Tinea cruris; Voriconazole.

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Introduction

Tinea cruris is a significant and increasingly challenging public health concern in tropical and subtropical regions globally. Such conditions are

mainly caused by dermatophytes, which flourish in warm and humid conditions facilitated by factors such as poor hygiene, occlusive clothing, and immunocompromised states. There has been a prominent epidemiological shift towards chronic and recurrent types of dermatophytosis, collectively referred to as recalcitrant tinea cruris, which has complicated conventional therapeutic approaches and raised severe concerns regarding antifungal resistance.¹⁻⁴

Address for correspondence

Dr. Murad Ali, Postgraduate Resident
Department of Dermatology,
Lady Reading Hospital, Peshawar.
Email: dr.muradali0305@gmail.com

Terbinafine has been broadly regarded as a first-line therapy because of its fungicidal activity against dermatophytes. Emerging evidence suggests a deteriorating efficacy of terbinafine in cases of recalcitrant dermatophytosis, attributed mainly to the development of resistance mechanisms in dermatophyte species.^{5,6} A study highlighted that terbinafine-resistant *Trichophyton tonsurans* leads to persistent tinea cruris with high minimum inhibitory concentrations, displaying reduced terbinafine susceptibility. This rising resistance trend has additionally been verified by clinical data showing suboptimal cure rates even with extended treatment durations of terbinafine. The clinical manifestation of recalcitrant tinea cruris has evolved and is characterized by extensive lesions and recurrent relapses regardless of sufficient treatment.⁷⁻⁹ Clinicians are thus challenged with therapeutic dilemmas, demanding the exploration of alternative antifungal agents with broader spectra and enhanced efficacy.

Voriconazole in recent times has attracted attention in the management of resistant dermatophytic infections. Its mechanism of action confers potent activity against a broad range of fungal pathogens, including dermatophytes.^{10,11} A study conducted in Pakistan showed an efficacy rate of 82% in patients managed with voriconazole, including those with resistant infections.¹² Such data emphasize voriconazole as a salvage treatment in difficult cases, although concerns regarding cost and safety remain to be fully addressed.^{12,13}

The rising rate of recalcitrant tinea cruris has become a noteworthy therapeutic challenge worldwide. Terbinafine is increasingly associated with prolonged disease courses, mainly attributed to developing antifungal resistance. Voriconazole has demonstrated promising activity against resistant dermatophyte strains and may provide a viable therapeutic option. Despite its growing clinical use, there remains a dearth of comparative evidence assessing the effectiveness of terbinafine versus voriconazole in cases of recalcitrant tinea cruris.

This study was therefore rationalized to generate evidence-based data to guide clinicians in selecting appropriate antifungal treatments, optimizing patient outcomes, and addressing the rising burden of resistant dermatophytic infections. The aim of this study was to compare the efficacy of terbinafine versus voriconazole in treating recalcitrant tinea cruris.

Methods

The comparative prospective cohort study was conducted on 300 patients in the Department of Dermatology, Lady Reading Hospital, Peshawar from March 2025 to January 2026. Ethical approval was obtained from the Institutional Review Board (IRB) of the institute (Ref. No. 279/LRH/MTI dated 08.08.2024). Prior to enrolment, written informed consent was obtained from all patients, accompanied by a detailed explanation of research protocols. Comprehensive medical histories and thorough physical examinations were performed. The sample size (300) was calculated using the World Health Organization sample size calculator, keeping a 5% level of significance, 80% power of test, and an expected efficacy of 83.3% in the voriconazole group¹⁴ and 74.3% in the terbinafine group.¹⁵ A non-probability consecutive sampling technique was employed.

Patients aged between 20 and 70 years of either gender who had a confirmed diagnosis of recalcitrant tinea cruris were included in the study. Tinea cruris was classified as recalcitrant if it failed to respond to one month of standard initial topical antifungal medication despite adherence.¹⁶ The diagnosis of tinea cruris was established through clinical examination and confirmed by microbiological analysis. A 10% potassium hydroxide (KOH) mount was employed for direct microscopy of skin scrapings. Each smear underwent thorough examination at 400× magnification. Patients with immunocompromised states, active liver, renal, or cardiac diseases, history of hypersensitivity to terbinafine or voriconazole, and pregnant/ lactating women were excluded.

Baseline investigations, including Liver Function Tests (LFTs), Renal Function Tests (RFTs), and skin scrapings for 10% KOH microscopy, were conducted. Upon completion of baseline assessments, patients were assigned equally to either the voriconazole or terbinafine treatment group. Baseline photographic documentation was conducted

Patients were allocated to treatment groups in a 1:1 ratio using an alternate assignment method based on their order of enrolment with the consecutive patients sequentially assigned to Group A (Voriconazole) and Group B (Terbinafine). Group A received oral voriconazole 400 mg once daily while Group B received oral terbinafine 250 mg twice daily for four weeks. Treatment allocation were not randomised and treatment were determined as per the treating dermatologist's clinical decision. Efficacy assessment and mycological evaluation were performed independently where feasible to minimise the assessment bias

Treatment efficacy was assessed based on complete resolution, determined through clinical examination conducted by the researcher under the supervision of the primary consultant at 8 weeks post-therapy. A lesion was considered completely resolved if there were no active borders, scaling, inflammatory changes, or associated itching, accompanied by a negative 10% KOH test result. Partial resolution was evaluated at 8 weeks post-therapy and defined as lesions displaying hyperpigmentation with distinct macules and papules with persistent itching, despite a negative 10% KOH test.¹⁷ 'No change' was defined as lesions maintaining visual resemblance to baseline observations. Severity of disease was measured using criteria established by Naseer *et al.* classifying cases as mild, moderate, or severe.¹⁷

Patients underwent treatment for 4 weeks. Adverse events were assessed during the weekly follow-up visits throughout the 4-week treatment period and at the 8 week efficacy assessment was performed through patient clinical examination. Management of side effects included symptomatic treatment for mild

events while severe adverse effects prompted immediate drug discontinuation and specialist referral. Efficacy was assessed at 8 weeks post-treatment initiation (4 weeks after treatment completion) to allow sufficient time for complete clinical and mycological resolution and to evaluate the durability of treatment response.

Data were analyzed using SPSS version 25. Numerical variables such as age and duration of disease were presented as median (IQR), after assessing for normality using the Shapiro-Wilk test. Categorical variables such as efficacy, comorbidities, family history of disease, disease severity, side effects, and gender were presented as frequencies and percentages. The chi-square test was used for comparison of efficacy between groups, with a P -value $\leq .05$ considered statistically significant.

Result

Three hundred patients with recalcitrant tinea cruris were enrolled in this study, with 150 patients assigned to each treatment group. Baseline profile of both groups alongwith the distribution of comorbidities, family history, and disease severity is detailed in **Table 1**.

Table 1 Baseline profile of the patients (N = 300)

Baseline Parameter	Group A (n=150) (Voriconazole)		Group B (n=150) (Terbinafine)	
	n	%	n	%
Gender				
Male	78	52.0%	82	54.7%
Female	72	48.0%	68	45.3%
Diabetes				
Yes	16	10.7%	18	12.0%
No	134	89.3%	132	88.0%
Hypertension				
Yes	22	14.7%	27	18.0%
No	128	85.3%	123	82.0%
Family History				
Yes	12	8.0%	9	6.0%
No	138	92.0%	141	94.0%

Age (Years), Median (IQR): Group A = 30 (26.50–38); Group B = 33 (27–43)

Disease Duration (Months), Median (IQR): Group A = 10 (6–13); Group B = 9 (7–12)

Table 2 Efficacy of treatment between both groups at 8 weeks.

Efficacy Category	Group A (Voriconazole) (n=150)		Group B (Terbinafine) (n=150)		P-value*
	n	%	n	%	
Complete Resolution	122	81.3%	95	63.3%	<.001
Partial Resolution	21	14.0%	36	24.0%	.028
No Change	7	4.7%	19	12.7%	.014
Overall Response Difference					< .001

*Chi-square test used for categorical comparisons.

Table 3 Comparison of adverse effects between treatment groups.

Side Effect	Group A (Voriconazole) (n=150)		Group B (Terbinafine) (n=150)		P-value*
	n	%	n	%	
Nausea	12	8.0%	9	6.0%	.491
Visual Disturbances	9	6.0%	2	1.3%	.032
Jaundice	6	4.0%	4	2.7%	.521
Skin Rash	5	3.3%	3	2.0%	.473
No Side Effects	118	78.7%	132	88.0%	.161

*Chi-square test.

Efficacy was evaluated at 8 weeks post-treatment initiation. In the voriconazole group, 122 patients (81.3%) achieved complete resolution, whereas among patients treated with terbinafine, 95 (63.3%) achieved complete resolution ($P < .001$) (**Table 2**). Table III presents the safety profile; no statistically significant difference in side effect incidence was observed between groups ($P = .161$).

Discussion

The present study examined the efficacy of voriconazole and terbinafine for the management of recalcitrant tinea cruris among 300 patients. The median age of patients was comparable between groups (30 years in Group A vs. 33 years in Group B). These findings are consistent with Naseer *et al.* who documented a mean age of 35.1 ± 11.1 years, validating that dermatophytosis predominantly affects young and middle-aged adults.¹⁷ The demographic profile further demonstrated a male predominance in both groups (52.0% vs. 54.7%), aligning with Akter *et al.* who reported 54.0% male involvement in their voriconazole group and 56.0% in their terbinafine group.¹⁸ Similarly, Das *et al.* noted a peak prevalence of dermatophytosis among adults aged 18 to 40 years.¹⁹

The median disease duration in both groups was 9 to 10 months, corresponding well with findings by

Akhter *et al.* who reported similar infection durations in recalcitrant cohorts.²⁰

Efficacy analysis demonstrated that voriconazole achieved a complete resolution rate of 81.3% ($n=122$), significantly outperforming terbinafine (63.3%, $n=95$; $P < .001$). These results mirror Akter *et al.* who reported an 82% complete cure rate with voriconazole versus 64% with terbinafine in 100 patients with relapsed/ resistant tinea.¹⁸ Consistency across studies strongly reinforces voriconazole's superior efficacy in recalcitrant dermatophytosis. Furthermore, Naseer *et al.* observed an 85.5% complete cure rate with voriconazole in a single cohort study.¹⁷

Partial resolution occurred in 14.0% ($n=21$) of voriconazole-treated patients versus 24.0% ($n=36$) in the terbinafine arm, illustrating distinct clearance dynamics. Akter *et al.* similarly noted partial improvement in 14.5% of voriconazole and 20.0% of terbinafine cases.¹⁸ Higher partial resolution with terbinafine indicates that while fungal burden may be reduced, post-inflammatory changes and persistent symptoms frequently linger, reflecting incomplete fungal clearance.

Our findings must be interpreted in the context of emerging global antifungal resistance. Tan *et al.* identified *Trichophyton indotineae* harboring the

Leu393Ser point mutation in the squalene epoxidase gene in recalcitrant cases, driving high terbinafine minimum inhibitory concentrations.²¹ This genomic resistance mechanism explains terbinafine's declining cure rates. Additionally, Khan *et al.* reported that 91.7% of dermatologists globally encountered recalcitrant or recurrent tinea over a 3-year period, predominantly driven by Trichophyton mentagrophytes and Trichophyton rubrum.²² Rampant misuse of topical corticosteroid-antifungal combinations further exacerbates atypical presentations and therapeutic failure.

Regarding safety, voriconazole caused visual disturbances in 6.0% of patients compared to 1.3% in the terbinafine group ($P=.032$), whereas nausea was common in both arms. Overall adverse events showed no overall statistical difference between cohorts ($P=.161$). Bibi *et al.* reported transient visual disturbances in 10% of voriconazole recipients.²³

A major strength of this study is its robust head-to-head design and larger sample size ($n=300$) compared to previous literature, providing strong statistical power. Limitations include a single-center design and the lack of molecular species identification and mycology MIC testing. Future multi-center studies integrating genomic surveillance are recommended.

Conclusion

Voriconazole demonstrated significantly superior efficacy compared to terbinafine in achieving complete resolution of recalcitrant tinea cruris at 8 weeks post-treatment, with a comparable safety profile. Voriconazole represents a highly effective alternative for patients failing standard terbinafine therapy.

Declaration of patient consent Authors certify that they have obtained all appropriate patient consent.

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Conflict of interest No conflict of interest.

Author's contribution

MA: Substantial contribution to the conception and study design, acquisition, analysis and interpretation of data.

SMN: Contribution to study design, critical review of the manuscript.

SJ: Contribution to study design, manuscript writing.

BA: Substantial contribution to conception and study design, critical review of the manuscript.

S: Substantial contribution analysis and interpretation of data, manuscript writing.

Every author has given final approval of the manuscript version to be published and agreed to be accountable for all aspects of the work.

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