Original Article

Efficacy and Safety of Voriconazole in the Treatment of Tinea Corporis and Cruris Infections

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Abstract

Background: The World Health Organization estimates that dermatophytes affect approximately 25% of the global population, indicating their widespread prevalence and impact on public health. Voriconazole, a newer second-generation triazole antifungal agent, has shown promise as an alternative treatment option for dermatophytosis.

Objective: The objective of this study was to evaluate the efficacy and safety of Voriconazole in treating Tinea Corporis and Cruris.

Methods: This single-center observational study enrolled 227 eligible participants aged between 18 and 70 years after providing written informed consent. Participants were categorized into new cases, resistant cases, and relapsing cases based on specific criteria. Baseline evaluations were conducted, including safety and disease assessments, before treatment initiation. Severity grading was noted for each patient. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS ver. 23).

Results: Demographics revealed a male predominance (59%), with a mean age of 35.1 $\pm$ 11.1 years. Most participants were unmarried (54.2%) and had no family history of the disease (66.1%). Majority were new cases (66.1%) with moderate disease severity (55.9%). Voriconazole therapy at week 12 resulted in an 85.5% "Complete Cure" response, with higher efficacy in males (61.3%) and younger age groups (58.2% aged 18-40 years). Side effects included nausea (8.8%) and vomiting (5.7%).

Conclusion: The study concludes that voriconazole is effective for treating Tinea Corporis and Tinea Cruris infections, especially in new cases and those with mild to moderate severity. With an 85.5% complete cure rate at the 12-week assessment, voriconazole demonstrates promising efficacy, along with manageable side effects.

Keywords: Voriconazole, Dermatophytosis, Antifungal, Efficacy, Safety, Voriconazole.

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Introduction

The World Health Organization estimates that dermatophytes affect approximately 25% of the global population, indicating their widespread prevalence and impact on public health.[1,2] Factors such as high humidity, overpopulation, and poor hygiene contribute to the dissemination of dermatophyte infections, particularly in regions with hot

and humid climates.[3-6] In Bangladesh, where environmental conditions favor fungal growth, dermatophytosis is notably common, posing a significant burden on healthcare systems and individuals alike.[7]

Traditionally, dermatophytosis was effectively managed with topical or systemic antifungal agents.[8,9] However, the emergence of drug-resistant strains has complicated treatment outcomes, leading to treatment failures and recurrent infections.[10-12] Notably, resistance to commonly used oral antifungal drugs like fluconazole, itraconazole, and terbinafine has been observed, necessitating the exploration of alternative treatment strategies.[13-15]

Voriconazole, a newer second-generation triazole antifungal agent, has shown promise as an alternative treatment option for refractory cases of dermatophytosis.[16] With its broad-spectrum antifungal activity and approval for the treatment of invasive fungal infections, voriconazole presents a potential solution to the growing challenge of drug-resistant dermatophyte infections.[17] However, the clinical efficacy and safety of oral voriconazole specifically for dermatophytosis remain underexplored, with limited literature available on its use in this context.[18,19] Given the rising incidence of drug-resistant dermatophyte infections and the need for effective therapeutic options, further research is warranted to evaluate the efficacy and safety of oral voriconazole in managing tinea corporis and cruris infections.[20]

Several studies have been conducted across different countries to assess the effectiveness of Voriconazole in treating Tinea Corporis and Cruris infections. However, in Pakistan, there is a notable absence of local data despite dermatophytosis being a prevalent issue and cases of resistance to existing therapies on the rise. By addressing these gaps in understanding, we can improve treatment outcomes and reduce the burden of dermatophyte infections on affected individuals and healthcare systems. Thus, this study aimed to investigate the efficacy and safety of Voriconazole in treating Tinea Corporis and Cruris infections specifically in the interior Sindh region of Pakistan.

Methods

This single center, observational study aimed to assess the efficacy and safety of Voriconazole in treating Tinea Corporis and Cruris infections across interior Sindh. The study involved a baseline visit and treatment follow-up period. A total of 227 eligible study subjects were enrolled from the study center after signing a written informed consent. The sample size, calculated using OpenEpi version 3 with a 95% confidence level, a 5% margin of error, and an assumed efficacy of 80% for voriconazole in treating Tinea corporis and Tinea cruris based on Shahzad et al, (2022),[19] required 227 participants. Patients were selected through a non-probability consecutive sampling method. Inclusion criteria for this study comprised individuals aged between 18 and 60 years diagnosed with dermatophyte infections (specifically Tinea Corporis and Cruris), regardless of lesion size. Participants were required to be in good overall health based on a review of their medical history, willing to comply with the study protocol for applying test materials, and capable of understanding and providing written informed consent. On the other hand, exclusion criteria encompassed patients with chronic immunosuppressive conditions such as diabetes, malignancy, liver or renal disease, tuberculosis, AIDS, history of organ transplant, or prior immunosuppressive therapy. Additionally, females who were pregnant or nursing during the study period were excluded. Individuals resistant to any antifungal treatment, those with conditions deemed inappropriate for study participation by the investigator, and those with a history of hypersensitivity to Voriconazole were also excluded from the study.

During the study, patients were categorized into three groups: new cases, resistant cases, and relapsing cases based on specific criteria. New cases referred to patients with no history of Tinea Corporis or Cruris in the last three months. Resistant cases were those who had undergone at least two weeks of oral antifungal treatment with Terbinafine or Itraconazole without recovery. Relapsing cases included patients who experie-

nced Tinea Corporis or Cruris, received treatment, experienced lesion healing, and then suffered a recurrence within the last three months.

At baseline, all patients underwent evaluation for eligibility criteria, completing required baseline safety and disease assessments before treatment initiation. Detailed efficacy and safety data were collected throughout the study period. In assessing dermatophytosis severity, we are applying the criteria outlined by Ahmed et al, (2022). This approach involves a detailed skin examination, where clinical signs like itching (pruritus), scaling, and redness (erythema) are rated based on a 4-point scale. According to this scale, each symptom is scored from 0 to 3, with 0 indicating no symptoms, 1 as mild, 2 as moderate, and 3 as severe, reflecting the intensity of each clinical feature observed in the patients.[16] Each patient received an oral dose of voriconazole at 200 mg twice daily for a period of two weeks. Follow-up assessments were conducted at the end of weeks 2, 4, and 12, with efficacy specifically evaluated at the 12-week. In the study by Khattab et al, (2022), clinical response was categorized into two levels: a complete clinical cure, characterized by the full disappearance of skin lesions, leaving normal-looking skin, and an incomplete clinical cure, where only partial improvement of the skin lesions was observed.[29]

The Statistical Package for Social Sciences (SPSS ver. 23) was utilized for both data entry and statistical analysis in this study. Descriptive and inferential statistics were employed to analyze the data. For categorical variables, numbers and frequencies were calculated, while means and standard deviations were computed for numerical variables. The chi-square test was employed to determine associations between groups and efficacy, with a significance level set at $p < 0.05$.

Results

In the study evaluating the efficacy and safety of Voriconazole in treating Tinea Corporis and Cruris infections in the interior Sindh region, a total of 227 participants were enrolled. All patients successfully completed the study, with no recorded dropouts. Demographic and clinical characteristics of the participants are summarized in Table 1. Of the participants, 134 (59%) were female, while 93 (41%) were male, with a mean age of 35.1 ± 11.1 years. Marital status distribution showed that 104 (45.8%) were married, and 123 (54.2%) were unmarried. Family history of the disease was reported by 77 (33.9%) participants, whereas 150 (66.1%) had no family history. Occupationally, the participants varied, with 82 (36.1%) being students, 64 (28.2%) housewives, 64 (28.2%) healthcare workers, and 17 (7.5%) falling into the "Others" category.

Regarding diagnosis, 123 (54.2%) participants had Tinea Corporis, 77 (33.9%) had Tinea Cruris, and 27 (11.9%) had both conditions. The duration of illness ranged from less than 6 months for 68 (30%) participants, 6 months to 1 year for 114 (50%), and more than 1 year for 45 (20%). The study population included various case types, with 150 (66.1%) classified as new cases, 45 (19.8%) as resistant, and 32 (14.1%) as relapsing. Disease severity distribution showed that 36 (15.9%) had mild disease, 127 (55.9%) had moderate disease, and 64 (28.2%) had severe disease.

Figure 1 depicted the response to Voriconazole therapy at week 12 among the 227 participants enrolled in the study. The results revealed that 194 (85.5%) individuals were classified as "Complete Cure" at the 12-week. Additionally, 28 (14.5%) participants were categorized as "Partial Cure".

Table 2 provided a comprehensive comparison of Voriconazole's efficacy across various demographic and clinical parameters among the 194 fully cured participants in the study. Analysis of the data indicated that 119(31.3%) of males and 75(38.7%) of females achieved a complete cure with Voriconazole treatment (p=0.086). Moreover, participants aged 18-40 years exhibited a higher rate of complete cure 113(58.2%) compared to those aged 41-60 years 81(41.8%) (p=0.090). However, no significant difference in efficacy was observed between married 89(45.9%) complete cure and unmarried 105(54.1%) complete cure participants (p=0.964). Similarly, participants with or without a family history of the disease showed

efficacy rates of 62(32%) and 132(68%) complete cures, respectively (p=0.130).

Table 1: *Demographics & Clinical Profile of Study Participants (n=227)*

Gender	
Male	134(59%)
Female	93(41%)
Age (years)	
Mean ± SD	35.1 ± 11.1
Marital Status	
Married	104(45.8%)
Unmarried	123(54.2%)
Family History	
Yes	77(33.9%)
No	**150(66.1%)**
Occupation	
Student	82(36.1%)
Housewife	64(28.2%)
Healthcare Workers	64(28.2%)
Others	17(7.5%)
Diagnosis	
Tinea Corporis	**123(54.2%)**
Tinea Cruris	77(33.9%)
Both	27(11.9%)
Duration of Illness	
< 6 months	68(30%)
6 months – 1 Year	**114(50%)**
> 1 Year	45(20%)
Types of Cases	
New	**150(66.1%)**
Resistant	45(19.8%)
Relapsing	32(14.1%)
Severity of Disease	
Mild	36(15.9%)
Moderate	**127(55.9%)**
Severe	64(28.2%)

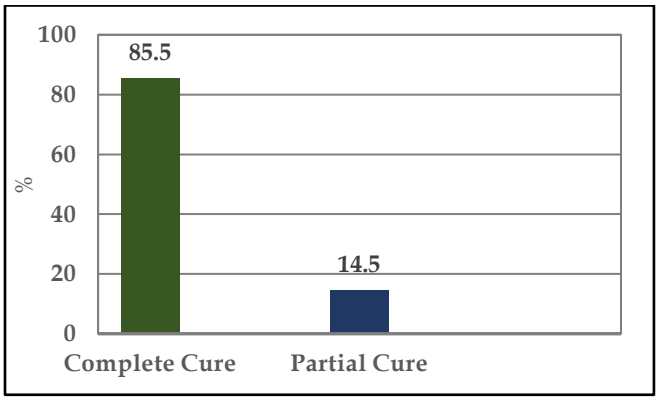

Figure 1: *Response to Therapy with Variconazole at Week 12(n=227).*

The type of dermatophyte infection (Tinea Corporis or Tinea Cruris) did not significantly affect Voriconazole's efficacy, with efficacy rates of 107(55.2%) and 67(34.5%), respectively (p=0.202). However, participants with a duration of illness (6 months-1 year) demonstrated a higher efficacy rate 106(54.6%) complete cure compared to those with shorter durations (<6 months) 59(30.4%) complete cure and over 1 year: 29(15%) (p<0.001).

Table 2: *Comparison of Efficacy (Fully Cured) of Voriconazole with other Parameters (n=194)*

Variables	Efficacy (Fully Cured) n (%)	p-value
Gender		
Male (134)	119(61.3)	0.086
Female (93)	75 (38.7)	
Age (years)		
18 – 40 (127)	113(58.2)	0.090
41 – 60 (100)	81(41.8)	
Marital Status		
Married (104)	89(45.9)	0.964
Unmarried (123)	105(54.1)	
Family History		
Yes (77)	62(32)	0.130
No (150)	132(68)	
Diagnosis		
Tinea Corporis (123)	107(55.2)	0.202
Tinea Cruris (77)	67(34.5)	
Both (27)	20(10.3)	
Duration of Illness		
< 6 months (68)	59(30.4)	<0.001
6 months – 1 Year (114)	106(54.6)	
> 1 Year (45)	29(15)	
Types of Cases		
New (150)	138(71.1)	<0.001
Resistant (45)	36(18.6)	
Relapsing (32)	20(10.3)	
Severity of Disease		
Mild (36)	34(17.5)	0.194
Moderate (127)	108(55.7)	
Severe (64)	52(26.8)	

*Chi square test, p-value (2-tail), p<0.05 significant

Furthermore, new cases exhibited the highest efficacy rate 131(71.1%) complete cure, followed by resistant cases 36(18.6%) complete cure and relapsing cases 20(10.3%) (p<0.001). Additionally, participants with moderate disease severity showed the highest efficacy rate 108(55.7%) complete cure, followed by severe 52(26.8%) complete cure and mild 34(17.5%) complete cure cases (p=0.194).

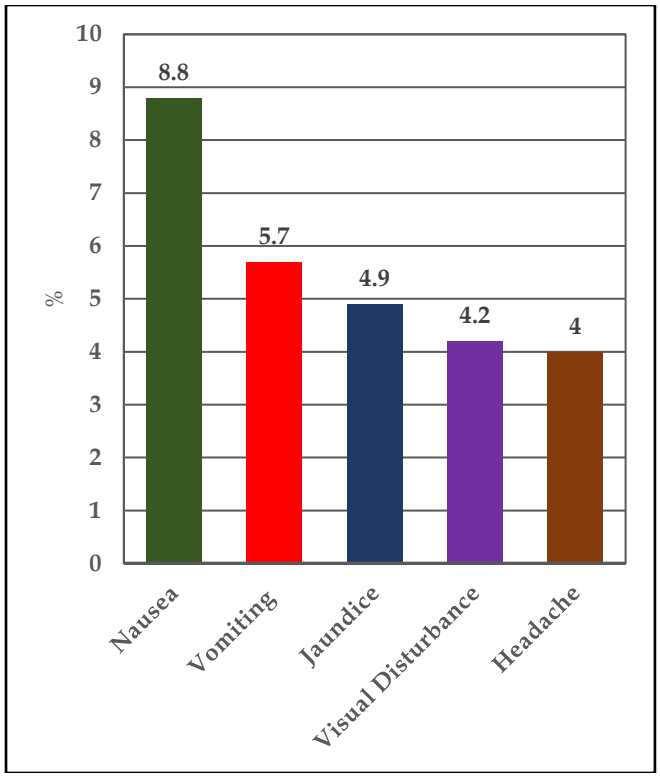

Figure 2: *Side Effects Reported by Study Participants at the End of Study (n=227).*

Figure 2 presented an overview of the side effects reported by the 227 study participants. Among the reported side effects, nausea was the most commonly noted, affecting 8.8% of participants. Following closely, vomiting was reported by 5.7% of the participants, while jaundice was observed in 4.9% of participants. Visual disturbances and headache were reported by 4.2% and 4.0% of individuals, respectively.

Discussion

In this study, we investigated the efficacy and safety of Voriconazole in treating Tinea Corporis and Cruris infections in the interior Sindh region. Our findings reveal several important insights into the management of dermatophyte infections, aligning with and expanding upon previous research.

Our study observed a predominance of male participants (59%), consistent with studies by Brigida et al[21] and Ganage et al,[22] which reported similar gender distributions in dermatophyte infections. This gender disparity underscores the need for targeted interventions and emphasizes the importance of considering gender-specific factors in disease management strategies.

The age distribution of participants in our study mirrors findings from Das et al,[23] indicating a higher prevalence of dermatophyte infections among individuals aged 18-40 years. This demographic trend highlights the vulnerability of young to middle-aged adults to dermatophyte infections and underscores the importance of targeted prevention efforts in this age group.

Comparison with Khondker et al,[24] and Kafi et al,[25] suggests that Voriconazole demonstrates superior efficacy compared to other antifungal agents, particularly in new cases of dermatophytosis. Our study found a high efficacy rate (85.5% complete cure) with Voriconazole treatment in new cases, indicating its potential as a first-line therapeutic option in regions with high rates of antifungal resistance.

Regarding disease severity, our study observed a lower proportion of participants with severe disease compared to Kafi et al,[25] suggesting potential regional variations in disease burden and severity. This variability underscores the importance of tailoring treatment approaches to account for regional differences in disease presentation and progression.

In terms of treatment response, our study found varying cure rates across different patient subgroups, consistent with Majid et al[26] and Sharma et al,[27] who reported similar variability in treatment outcomes with other antifungal agents. These findings emphasize the importance of personalized treatment approaches based on factors such as disease severity, duration, and patient demographics.

Furthermore, our study and discussions with Khatri et al,[28] highlight the emergence of antifungal resistance as a significant concern in the management of dermatophyte infections. While Voriconazole showed high efficacy in our study, other commonly used antifungal agents such as

fluconazole and terbinafine exhibited higher rates of resistance in previous studies.

The safety profile of Voriconazole observed in our study aligns with findings from discussions with Das et al[24] and Majid et al,[27] indicating manageable side effects such as nausea, vomiting, and visual disturbances. Understanding the safety profile of antifungal medications is crucial for guiding treatment decisions and optimizing patient outcomes.

This study's limitations include its single-center design, which restricts the findings' applicability to broader populations and settings. Conducting the study at only one location may not capture variations in patient characteristics, healthcare practices, or environmental factors present in other regions, thereby limiting the generalizability of the results. Additionally, while efficacy was evaluated at 12 weeks, a longer follow-up period would be beneficial to assess sustained effectiveness and monitor recurrence rates, as dermatophyte infections can have high relapse potential.

Conclusion

The study concludes that voriconazole is effective for treating Tinea Corporis and Tinea Cruris infections, especially in new cases and those with mild to moderate severity. With an 85.5% complete cure rate at the 12-week assessment, voriconazole demonstrates promising efficacy, along with manageable side effects.

Ethical Approval: The study was approved by Ethical Review Committee vide letter no ,PUMHSW/SBA/PVC/2023/294.

Conflict of Interest: There was no conflict of interest to be declared by any author.

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Author's Contribution

MN: Study design, data collection, drafting and critical review, final approval.
VD: Study design, data collection, drafting and critical review.
T: Data Collection, drafting of article.
KNK: Study design, data collection, drafting and critical review, final approval.
NA: Data Collection, drafting of article.
AA: Analysis and interpretation.
MIA: Drafting of Article.
NM: Data collection, analysis and interpretation.
AA: Study design, data collection, drafting and critical review, final approval.
MAK: Is the professional medical writer, for data management, analysis and writing assistance

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