

EFFICACY AND SAFETY OF VORICONAZOLE IN THE TREATMENT OF TINEA CORPORIS AND CRURIS INFECTIONS

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ABSTRACT

Background: Dermatophytosis is a frequent superficial fungal infection in a large segment of the world's population. Conventional anti-fungals have become less effective due to increased resistance and recurrent infections, therefore other systemic anti-fungals like voriconazole are needed.

Objective: To evaluate the efficacy and safety of oral voriconazole in the treatment of tinea corporis and tinea cruris infections.

Methods: The present study was done in the Department of Dermatology, Shaheed Mohtarma Benazir Bhutto Medical University Hospital at Larkana for a period of six months. Patients aged 18–60 years with clinically diagnosed tinea corporis and/or tinea cruris were consecutively sampled and a total of 98 patients were enrolled. All patients were treated with oral voriconazole 200 mg twice daily for 28 days and followed up at 2, 4 and 12 weeks. The efficacy of the treatment was evaluated by complete and incomplete clinical cure, and safety was evaluated by adverse effects. Data was analyzed using SPSS version (25).

Results: The average age of the subjects was 34.7 ± 10.2 years and males accounted for 62.2% of the study population. The most common symptom was pruritus. At 12 weeks follow up, complete clinical cure was obtained in 85.7% of the patients and incomplete clinical cure was obtained in 14.3% of the patients. Few patients experienced mild adverse reactions such as headache, nausea, blurred vision, rash and vertigo, none of which were serious.

Conclusion: Oral voriconazole showed good efficacy and tolerability in the treatment of tinea corporis and tinea cruris infections. The results indicate that voriconazole could be a valuable therapeutic alternative in resistant or recurrent dermatophytosis. Further studies with larger numbers of centres are recommended to confirm these results.

KEYWORDS: Dermatophytosis; Tinea Corporis; Tinea Cruris; Voriconazole; Antifungal Therapy; Dermatophyte Infections; Clinical Cure; Drug Resistance.

INTRODUCTION:

Dermatophytosis is a highly infectious superficial skin fungal disease with a global distribution of infected individuals of 20-25%; especially affected populations are in the Tropics and developing countries {1}. In dermatology, the most common examples are tinea corporis and tinea cruris. Tinea corporis elicits an infection of the trunk, extremities, and the neck. In tinea cruris pruritus, erythema, and scaling occurs in the groin, and involves the surrounding regions, ultimately resulting in significant deterioration of the quality of life {2,3}. Concern exists regarding chronic, recurrent, and stubborn dermatophytosis epidemiological studies targeting South Asian countries due to irrational use of corticosteroids, poor sanitation, and congested living combined with inappropriate antifungal treatment {4,5}.

Fungi that cause dermatophytosis belong to the genera *Trichophyton*, *Microsporum*, and *Epidermophyton* with the abundant *Trichophyton mentagrophytes* and *Trichophyton rubrum* as the most frequently implicated pathogens in resistant infections {6}. Concerning status of emerging antifungal resistance is a critical challenge when managing dermatophytosis and especially respect commonly used agents like terbinafine and fluconazole {7}. Therefore, interest is shifting to other systemic antifungal agents that are more likely to produce better clinical outcomes.

Voriconazole, belongs to the second-generation triazole group of antifungals, and is a potent antifungal agent against dermatophytes, exerting its fungus effect through the inhibition of the cytochrome P450-dependent synthesis of ergosterol {8}. Evidence from recent clinical studies seems promising for the use of oral voriconazole for cases of recalcitrant and recurrent dermatophytosis. Remarkable clinical and safety outcomes concerns for resistant dermatophyte infections have been documented by Chandrashekar and Poojitha for the voriconazole treatment {9}. Complete clinical cure of tinea corporis and cruris infections has been claimed by Naseer et al. to be in 85.5% of the patients post voriconazole {10}. Despite the promising results, there is a paucity of local data

concerning its efficacy and safety profile. The current study, therefore, intends to assess the efficacy and safety of voriconazole in patients suffering from tinea corporis and cruris.

METHODOLOGY:

After the College of Physicians and Surgeons Pakistan (CPSP) approved the Research Synopsis, this descriptive observational study was conducted over a period of six months at the Department of Dermatology, Shaheed Mohtarma Benazir Bhutto Medical University (SMBBMU) Hospital, Larkana, Pakistan. The study population included adult patients with clinically diagnosed tinea corporis and tinea cruris infections.

Using OpenEpi software, the sample size was estimated based on a previously reported complete clinical cure of 85.5%, assuming a 95% confidence interval, and a margin of error of 7%. Therefore, the minimum required sample size was 98 patients. A consecutive non-probability sampling technique was used for participant recruitment.

Patients of either gender, aged 18 to 60 years, diagnosed with tinea corporis or tinea cruris as per the operational definitions and who were provided oral voriconazole, were included in the study. Patients with a known history of hypersensitivity to voriconazole and chronic systemic illnesses including diabetes mellitus and hepatic, renal, malignant, or tuberculous illnesses, and acquired immunodeficiency syndrome, as well as those who had undergone organ transplant and those on immunosuppressive therapy, and those who were pregnant and/or lactating and those who were unwilling to participate, were excluded from the study.

Ethical approval was obtained from the CPSP Research Evaluation Unit. Informed consent was obtained from each patient. Both inpatient and outpatient participants from dermatology were recruited. A proforma was used to collect the data regarding age, sex, education, marital status, locus of residence, employment, family history of disease, length of disease, and presenting complaints. Clinical examination was carried out to confirm the diagnosis. Disease severity was assessed based on pruritus, scaling, and erythema, using a grading scale with a range of 0 – 3.

All the patients who were included in the study were given voriconazole, 200 mg, twice daily for 28 days. Three follow-up assessments were conducted at 2, 4, and 12 weeks post-initiation of the therapy. Clinical cures usually meant the complete clinical cure of skin lesions and complete normal appearance of the skin. Incomplete clinical cure was categorized accordingly. Safety of the drug was assessed based on the monitoring of the adverse effects and their documentation. Adverse effects were noted as nausea, vomiting, headache, blurred vision, rash, erythema, and vertigo.

The main variables of this study were the safety and efficacy of Voriconazole. Variables considered included age, sex, type and duration of disease, type of infection, clinical severity, and adverse drug reactions. Statistical Package for the Social Sciences version 25 was used for data analysis. For the continuous variables, age, and duration of disease, mean and standard deviation were calculated and for the discrete variables, sex, educational status, marital status, place of residence, occupation, diagnosis, severity, efficacy outcomes, adverse drug reactions and side effects were summarized as frequencies and percentages. Effect modifiers were addressed by stratification, and the chi-square test was performed post-stratification. A p value of ≤ 0.05 was considered statistically significant.

RESULT:

The study included 98 patients with tinea corporis and/or tinea cruris. The average age of the participants was 34.7 ± 10.2 years. 61 (62.2%) were males and 37 (37.8%) were females. Most participants were from the urban population. Demographic data is provided in Table 1.

Pruritus was the most common symptom presented by 92 (93.9%) of patients, followed by scaling in 76 (77.6%) and erythema in 69 (70.4%) patients. Tinea corporis was diagnosed in 44 (44.9%) patients, tinea cruris was diagnosed in 31 (31.6%) patients, and 23 (23.5%) patients were diagnosed with both. The data is further discussed in Table 2.

During follow up assessments, clinical improvement was noted. At the end of 12 weeks, 84 (85.7%) patients reached the endpoint of complete clinical cure, while 14 (14.3%) patients had not reached the endpoint of complete clinical cure. This is presented in Figure 1.

Minor adverse effects were noted in small number of patients. Headaches were reported by 9 (9.2%) patients, nausea in 7 (7.1%) patients, and blurred vision in 4 (4.1%) patients. Skin rashes were reported in 3 (3.1%) patients, and vertigo was reported in 2 (2.0%) patients, and there were no major adverse effects reported during the study. Safety data is presented in Table 3 and Figure 2.

Table 1. Demographic Characteristics of Study Participants

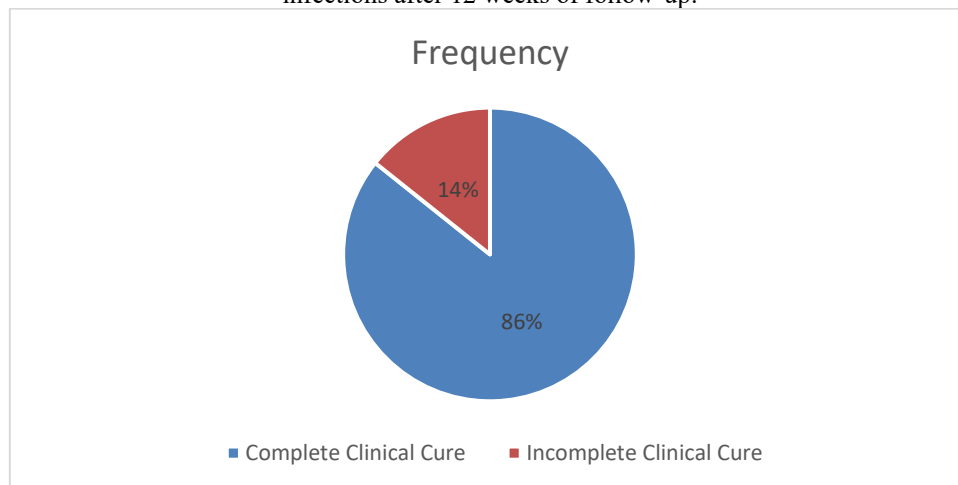
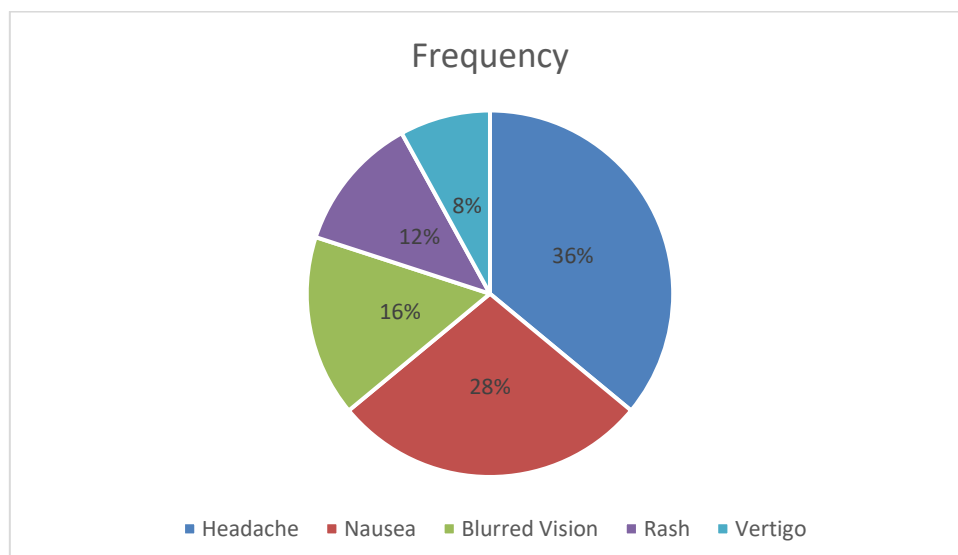
Variable	Frequency (n)	Percentage (%)
Male	61	62.2
Female	37	37.8
Urban Residence	63	64.3
Rural Residence	35	35.7
Married	58	59.2
Single	40	40.8

Table 2. Clinical Characteristics of Patients

Variable	Frequency (n)	Percentage (%)
Pruritus	92	93.9
Scaling	76	77.6
Erythema	69	70.4
Tinea Corporis	44	44.9
Tinea Cruris	31	31.6
Both Infections	23	23.5
Mild Severity	22	22.4
Moderate Severity	53	54.1
Severe Severity	23	23.5

Table 3. Adverse Effects Observed During Treatment

Adverse Effect	Frequency (n)	Percentage (%)
Headache	9	9.2
Nausea	7	7.1
Blurred Vision	4	4.1
Rash	3	3.1
Vertigo	2	2.0
No Significant Adverse Effect	73	74.5

Figure 1: Clinical cure outcomes among patients treated with oral voriconazole for tinea corporis and cruris infections after 12 weeks of follow-up.**Figure 2:** Frequency distribution of adverse effects observed in patients receiving oral voriconazole therapy for tinea corporis and cruris infections.

DISCUSSION:

Dermatophytosis is one of the most prevalent superficial global fungal infections, with certain modalities failing to adequately treat recurring cases with antifungal resistance occurrence {11,12}. The current research investigates tinea corporis and tinea cruris and assesses the consequences and the application of oral voriconazole. The results have shown favorable outcomes, and voriconazole is well tolerated. Voriconazole, a second-generation triazole, has been shown to achieve a high rate of clinical curing in resistant dermatophytosis {13,14}.

The occurrence of tinea among men and urban residents in this research reflects that observed by many regional epidemiological studies {15,16}. The increased prevalence in men and urban populations is attributed to close contact, increased sweating, and occupational exposure in overcrowded communities {17}. Consistent with numerous studies on the clinical manifestations of tinea cruris and corporis {18}, the most common clinical symptoms in this research were pruritus, erythema, and scaling.

The rise in the number of treatment failures with the standard antifungal drugs terbinafine and fluconazole has been linked with the resistance of skin fungal pathogens including the *Trichophyton mentagrophytes* complex. Research shows there have been changes in the cell membranes in conjunction with mutations in the squalene epoxidase genes that facilitate resistance to the action of the antifungal agent and allow the infection to persist. Evidence indicates that Voriconazole works by the prevention of membrane integrity of the fungal cell by inhibition of the 14 α demethylase enzyme of the Cytochrome P450 system of ergosterol and thus biosynthesis. The positive clinical outcomes with chronic and relapsing dermatophytosis patients can be related to the effectiveness of voriconazole, attributed to its broad antifungal coverage and the ability to penetrate tissues. Results from this study are congruent with those of Chandrashekar and Poojitha, wherein there was a considerable improvement from recalcitrant dermatophytosis after voriconazole was used systemically. Naseer et al. documented similar positive outcomes after the use of voriconazole to treat tinea corporis and tinea cruris. Clinical and mycological responses from refractory dermatophytosis after treatment with voriconazole by Ahmed et al. also showed similar positive outcomes.

In this study, adverse effects occurred infrequently, and if encountered, were mostly mild in nature, commonly presenting as headache and nausea. Similar findings have been reported in studies involving the use of systemic voriconazole in dermatophytosis {13,23}. Voriconazole-related adverse effects are generally of a mild and transient nature and consist of hepatic enzyme alterations, visual side effects, and gastrointestinal discomfort; however, significant toxicities are rare when treatment is carried out for limited periods of time under clinical oversight {24}. It is vital to carefully choose patients and monitor them to limit the adverse effects of the treatment. The present study's main strength was the ability to assess safety and efficacy in a population of patients suffering from dermatophytosis in a prospective fashion. Utilizing a structured approach to clinical evaluation and routinely scheduled visits markedly improved the reliability of the outcomes. Additionally, the study was able to address an important therapeutic concern in an area experiencing an increase in both recurrent and treatment resistant dermatophytosis.

Even with the aforementioned strengths, it is important to note a number of the study's limitations. The number of participants was small due to the study being undertaken at a single tertiary care center, which may impact the generalizability of the results. Fungal cultures and antifungal susceptibility testing were not undertaken, which may have limited the identification of the fungal species and resistance. Also, the lack of a comparative treatment group limited the ability to compare systemic antifungal treatments. Longer follow-up would have been helpful in assessing fungal recurrence after discontinuation of treatment.

The results from this study apply to a number of clinical situations. Voriconazole may be an effective treatment option for patients with recurrent, treatment-resistant, or difficult-to-treat dermatophytosis, particularly in areas where dermatophytosis is worsening due to an increase in antifungal resistance. For the evaluation and monitoring of voriconazole in dermatophyte infections, mycologically proven studies with control groups and larger sample sizes are warranted to address long-term safety concerns and any potential resistance development.

CONCLUSION:

The current study revealed a notable improvement in repigmentation for vitiligo patients who received combination therapy of topical tacrolimus and 308-nm excimer laser therapy as compared to patients who received topical tacrolimus alone. Patients who were part of the combination therapy had better clinical outcomes and grades of repigmentation. This advancement is possibly due to the combined effect of targeted phototherapy and immunomodulation which hastens and maintains the recovery of patient's melanocytes and stable vitiligo. It can be concluded that the combination therapy of excimer laser with tacrolimus is a treatment option for localized vitiligo. It is essential to conduct longitudinal and multi-site studies to further assess the frequency of this combination therapy and its efficiency in treatment.

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