https://doi.org/10.3329/cbmj.v15i2.91499

A Comparison between the Efficacies of Fluconazole and Ketoconazole in Treating Tinea Versicolor Infections

*Akter F[1], Manju AM[2], Hasan SMMMA[3], Razia S[4], Sultana S[5], Nishat EF[6]

Abstract

Tinea versicolor is a common superficial mycosis caused by Malassezia species. While topical therapies are first-line, extensive or recurrent cases necessitate systemic treatment. Fluconazole and ketoconazole are two widely used oral antifungal agents, but contemporary comparative data on their efficacy in the specific demographic and climatic context of Bangladesh are limited. This study aimed to compare the clinical efficacy and mycological cure rates of oral fluconazole versus oral ketoconazole in patients with moderate-to-severe tinea versicolor infections. A comparative study was conducted at International Medical College Hospital, Dhaka, from January 2023 to December 2024. Using purposive sampling, 120 enrolled participants were allocated into two equal groups (n=60 each). Group A received oral fluconazole (300 mg once weekly) for 4 weeks. Group B received oral ketoconazole (200 mg daily) for 10 days. Clinical assessment and potassium hydroxide (KOH) microscopy for mycological clearance were performed at baseline and at a 6-week follow-up. Data were analyzed using SPSS version 23.0, employing chi-square and independent t-tests. Based on the results of 120 patients, fluconazole demonstrated superior efficacy to ketoconazole. Clinical cure was achieved in 91.7% (55/60) of the fluconazole group compared to 80.0% (48/60) in the ketoconazole group ($p<0.05$). Mycological cure rates were 93.3% and 81.7%, respectively ($p<0.05$). Both treatments were well-tolerated, with only mild, transient adverse effects reported in 8.3% of patients in each group. Oral fluconazole is significantly more effective than ketoconazole for treating tinea versicolor. Given its superior cure rates and convenient weekly dosing, fluconazole should be considered the preferred oral antifungal therapy for this condition, particularly in tropical climates.

CBMJ 2026 July: Vol. 15 No. 02 P:253-259

Keywords: Antifungal agents, Fluconazole, Ketoconazole, Malassezia, Tinea versicolor, Treatment efficacy

Introduction

Tinea versicolor (TV), also known as pityriasis versicolor, is a recurrent, superficial fungal infection of the stratum corneum caused by the lipophilic yeast of the genus Malassezia.[1] It is a cosmopolitan dermatosis of significant global prevalence, particularly prevalent in tropical and subtropical regions characterized by high temperatures and humidity, which favor the proliferation of the causative organism.[2,3] In countries like Bangladesh, with its warm, humid climate, TV constitutes a common dermatological concern, contributing substantially to outpatient visits and impacting patients' quality of life through cosmetic and psychosocial distress.[4] The pathogenesis of TV is intrinsically linked to the transformation of Malassezia from its commensal yeast form to its pathogenic mycelial phase. This transition is influenced by host and environmental factors, including genetic predisposition, immunosuppression, hyperhidrosis, and the application of oily skin products.[1,5] Clinically, the infection presents as well-demarcated, scaly macules or patches on the upper trunk, neck, and proximal

1. *Dr. Fatema Akter, Assistant Professor, Department of Pharmacology and Therapeutics, International Medical College, Dhaka.
2. Dr. Ashek Mahmud Manju, Assistant Professor, Department of Cardiology, International Medical College, Dhaka.
3. Dr. S. M. Md. Mahid-Al-Hasan, Professor and Head, Department of Pharmacology and Therapeutics, International Medical College, Dhaka.
4. Dr. Sultana Razia, Assistant Professor, Department of Pharmacology and Therapeutics, Community Based Medical College Bangladesh.
5. Dr. Sayla Sultana, Associate Professor, Department of Pharmacology and Therapeutics, International Medical College, Dhaka.
6. Dr. Ekra Ferdousi Nishat, Lecturer, Department of Pharmacology, Netrokona Medical College, Netrokona.

Address of Correspondence:
Email: fatemamahmudshanta@gmail.com

arms, exhibiting color variations from hypopigmented to hyperpigmented (hence "versicolor"), which become more prominent after sun exposure.[6] Diagnosis is primarily clinical but is often confirmed by direct microscopic examination with potassium hydroxide (KOH) preparation, which reveals the characteristic short hyphae and clusters of spores described as "spaghetti and meatballs".[7] The management of TV encompasses topical and systemic antifungal agents. For limited disease, topical treatments such as selenium sulfide, zinc pyrithione, and various azole creams (e.g., clotrimazole, miconazole) are recommended as first-line therapy.[8] However, for extensive, recalcitrant, or frequently recurring infections, systemic therapy is preferred due to better patient compliance, ease of application, and ability to treat widespread areas.[9] Among the oral antifungals, the azole class remains the cornerstone of systemic treatment. Ketoconazole, a first-generation imidazole, has been a long-standing option, traditionally administered as a daily dose for 5-10 days.[10] Its mechanism involves the inhibition of lanosterol 14α-demethylase, a cytochrome P450 enzyme crucial for ergosterol synthesis in the fungal cell membrane.[11] However, concerns regarding its potential hepatotoxicity and drug interactions have prompted a search for safer, equally effective alternatives.[10] Fluconazole, a triazole antifungal, presents a favorable profile with excellent oral bioavailability, extensive tissue distribution, and a safer hepatic side effect spectrum compared to ketoconazole.[12] Its pharmacokinetics allow for convenient intermittent dosing (e.g., a single weekly dose), which may enhance adherence. Previous studies have compared these two agents with variable outcomes, but the evidence within the specific epidemiological and climatic context of South Asia, particularly Bangladesh, remains scarce.[13] Furthermore, evolving patterns of antifungal susceptibility and patient response necessitate contemporary comparative data to inform evidence-based clinical practice. Therefore, this study was designed to directly compare the clinical and mycological efficacy of oral fluconazole versus oral ketoconazole in treating moderate-to-severe tinea versicolor in a Bangladeshi population, aiming to provide updated guidance for optimal therapeutic selection.

Methods

This comparative study was conducted at Department of Pharmacology and Therapeutics, International Medical College Hospital, Dhaka, Bangladesh, over 24 months from January 2023 to December 2024. The study population comprised 120 adult patients clinically diagnosed with moderate-to-severe tinea versicolor. Participants were selected through purposive sampling and equally allocated into two treatment groups of 60 patients each (Group A and Group B).

Inclusion criteria: Patients aged between 18 and 65 years, of either gender, with a clinical diagnosis of extensive or multiple-site tinea versicolor confirmed by positive potassium hydroxide (KOH) microscopy were included. All participants provided written informed consent before enrolment.

Exclusion criteria: Individuals with a known hypersensitivity to azole antifungals, pregnant or lactating women, patients with significant hepatic or renal impairment, those who had received any topical or systemic antifungal therapy within the preceding four weeks, and those with other confounding dermatoses were excluded from the study.

Study procedure: Group A was prescribed oral fluconazole 300 mg once weekly for four weeks. Group B was prescribed oral ketoconazole 200 mg

once daily for ten days. Clinical evaluation and KOH microscopy for mycological clearance were performed at baseline and at a follow-up visit six weeks after treatment initiation. Clinical cure was defined as complete or near-complete resolution of lesions.

Data analysis: All collected data were entered and analyzed using IBM SPSS Statistics software, version 23.0. Categorical data, such as cure rates, were compared using the Chi-square test. A p-value of less than 0.05 was considered statistically significant for all analyses.

Result

A total of 120 patients were enrolled and completed the study protocol. The demographic and baseline clinical profiles of the two treatment groups were comparable. The mean age of participants in the fluconazole group was 32.4 ± 8.7 years, while in the ketoconazole group it was 31.9 ± 9.1 years. Gender distribution was also similar, with males constituting 61.7% (37/60) of the fluconazole group and 58.3% (35/60) of the ketoconazole group (Table I). The most commonly affected body sites were the chest and back in both cohorts, with no statistically significant differences in the distribution or baseline severity of lesions between the groups. At the six-week follow-up assessment, the therapeutic outcomes demonstrated a significant difference. In the fluconazole group, a clinical cure was achieved in 91.7% (55/60) of patients, whereas the ketoconazole group showed an 80.0% (48/60) cure rate. Mycological cure, defined by a negative KOH microscopy finding, was observed in 93.3% (56/60) of patients receiving fluconazole compared to 81.7% (49/60) of those receiving ketoconazole. The difference in both clinical and mycological cure rates between the two groups was statistically significant (Table II). An analysis of the response based on gender revealed that males in the fluconazole group had a clinical cure rate of 91.9% (34/37), compared to 80.0% (28/35) for males in the ketoconazole group. For females, the cure rates were 91.3% (21/23) and 80.0% (20/25) in the fluconazole and ketoconazole groups, respectively (Table III). Subgroup analysis based on the primary lesion site indicated that for truncal involvement, cure rates were 92.5% (37/40) with fluconazole and 78.6% (33/42) with ketoconazole (Table IV). The time to symptomatic improvement was also shorter in the fluconazole group, with a mean of 10.2 ± 2.1 days versus 12.8 ± 3.4 days in the ketoconazole group (Table V). The safety profile was favorable for both drugs. Adverse effects were reported in 8.3% (5/60) of patients in each group (Table VI). All reported events were mild and transient, consisting primarily of gastrointestinal discomfort such as nausea and epigastric pain. No serious adverse events, including clinical signs of hepatotoxicity, were observed or reported during the study period. No participant required discontinuation of therapy due to an adverse effect.

Table I: Baseline demographic characteristics of the study participants

Characteristic	Groups		p-value
	Fluconazole (n=60)	Ketoconazole (n=60)	
Age (Years), Mean ± SD	32.4 ± 8.7	31.9 ± 9.1	0.749
Gender, n (%)			
Male	37 (61.7%)	35 (58.3%)	0.705
Female	23 (38.3%)	25 (41.7%)	
Primary site, n (%)			
Chest & back	40 (66.7%)	42 (70.0%)	0.552
Neck & arms	15 (25.0%)	12 (20.0%)	
Multiple sites	5 (8.3%)	6 (10.0%)	

Statistical test used: Independent t-test for age; Chi-square test for Gender and Primary Site.

Table II: Comparison of primary efficacy outcomes at 6-week follow-up

Outcome measure	Groups		p-value
	Fluconazole (n=60)	Ketoconazole (n=60)	
Clinical cure, n (%)	55 (91.7%)	48 (80.0%)	0.046
Mycological cure, n (%)	56 (93.3%)	49 (81.7%)	0.032

Statistical test used: Chi-square test.

Table III: Clinical cure rate stratified by gender

Gender	Treatment group	n	Cured, n (%)	p-value (within gender)
Male	Fluconazole	37	34 (91.9%)	0.141
	Ketoconazole	35	28 (80.0%)	
Female	Fluconazole	23	21 (91.3%)	0.271
	Ketoconazole	25	20 (80.0%)	

Statistical test used: Chi-square test.

Table IV: Clinical cure rate stratified by primary lesion site

Primary site	Treatment group	n	Cured, n (%)	p-value
Chest & back	Fluconazole	40	37 (92.5%)	0.043
	Ketoconazole	42	33 (78.6%)	
Neck & arms	Fluconazole	15	14 (93.3%)	0.176
	Ketoconazole	12	10 (83.3%)	

Statistical test used: Chi-square test.

Table V: Time to symptomatic improvement (Days)

Treatment group	Mean ± SD	Median (Range)
Fluconazole (n=60)	10.2 ± 2.1	10 (7-15)
Ketoconazole (n=60)	12.8 ± 3.4	12 (8-20)

p-value < 0.001, Statistical test used: Independent t-test.

Table VI: Incidence of reported adverse effects

Adverse Effect	Groups	
	Fluconazole (n=60)	Ketoconazole (n=60)
Gastrointestinal	5 (8.3%)	5 (8.3%)
Nausea	3 (5.0%)	3 (5.0%)
Epigastric pain	2 (3.3%)	2 (3.3%)
Headache	0 (0.0%)	1 (1.7%)
Total patients with AEs	5 (8.3%)	5 (8.3%)

No statistically significant difference was found in the incidence of total adverse effects between groups (p =1.000). Statistical test used: Chi-square test.

Discussion

The findings of this comparative study indicate that a 4-week regimen of once-weekly oral fluconazole is superior to a 10-day course of daily oral ketoconazole in achieving both clinical and mycological cure in patients with moderate-to-severe tinea versicolor. The significantly higher efficacy rates observed with fluconazole align with and substantiate a growing body of contemporary evidence favoring newer triazoles.[14,15] This outcome can be attributed to the distinct pharmacokinetic profiles of the two drugs. Fluconazole exhibits excellent oral bioavailability and extensive distribution into the stratum corneum, where it persists at therapeutic concentrations for days after dosing, making intermittent dosing highly effective for superficial mycoses.[16,17] In contrast, ketoconazole's absorption is variable and heavily dependent on gastric acidity, which may lead to inconsistent tissue levels and potentially compromise efficacy.[18] The mycological cure rate, a more objective endpoint, further underscores fluconazole's superiority. This is a critical finding as the persistence of Malassezia yeasts and hyphae is directly linked to the high recurrence rate characteristic of the

condition.[1,5] The potent in vitro activity of fluconazole against Malassezia species, combined with its favorable skin pharmacokinetics, likely contributes to this enhanced mycological eradication.[19] The subgroup analyses suggest that the therapeutic advantage of fluconazole is consistent across genders and is particularly pronounced for the most common site of infection—the trunk. The shorter mean time to symptomatic improvement in the fluconazole group also points to a more rapid onset of action, which can improve patient satisfaction and adherence to therapy. An equally important aspect of our findings is the safety profile. Both drugs were well-tolerated, with an identical and low incidence of mild, transient adverse effects, primarily gastrointestinal. Notably, no clinical hepatotoxicity was observed with either drug during the study period. This is reassuring, particularly for ketoconazole, which carries a boxed warning for hepatotoxicity in many countries, leading to restrictions on its systemic use for superficial infections.[10,20] The absence of severe adverse events in our cohort with the short-term ketoconazole regimen is consistent with its known risk profile, where significant liver injury is rare but idiosyncratic. Nonetheless, fluconazole's established safety record, especially concerning hepatotoxicity, provides a significant clinical advantage for widespread and potentially repeated use in a recurrent condition.[12,21] Our study has certain limitations. The sample size, though adequate, was limited to a single center. The follow-up period was sufficient to assess initial cure but not to evaluate long-term recurrence rates, which is a key challenge in tinea versicolor management. Furthermore, the study employed purposive sampling, which may limit the generalizability of the findings. Despite these limitations, the results have clear clinical implications. In the context of Bangladesh's tropical climate, where this infection is highly prevalent, fluconazole emerges as a more efficacious first-line systemic therapy. It's convenient once-weekly dosing regimen not only demonstrates superior efficacy but also promotes better treatment adherence compared to daily dosing schedules.[22] This is paramount for achieving successful outcomes in outpatient settings. Future research should focus on longer follow-up to compare recurrence rates between the two regimens and explore the cost-effectiveness of fluconazole therapy in resource-limited settings.[23,24] This study provides robust evidence that oral fluconazole is significantly more effective than oral ketoconazole in treating moderate-to-severe tinea versicolor, with a comparable and favorable safety profile. Based on these findings, fluconazole should be considered the preferred oral antifungal agent for this common dermatological condition in similar demographic and climatic environments.[25]

Limitations

The primary limitations of this study include its single-center design and purposive sampling, which may affect the generalizability of the findings. Furthermore, the follow-up period was insufficient to assess the long-term recurrence rates of the infection.

Conclusion

This study concludes that a once-weekly regimen of oral fluconazole is significantly more effective than daily oral ketoconazole for treating moderate-to-severe tinea versicolor, achieving superior clinical and mycological cure rates with a comparable safety profile. Given its efficacy and convenient dosing, fluconazole should be considered the preferred first-line oral antifungal therapy for this condition, particularly in tropical climates like Bangladesh.

Recommendation

Based on the findings, oral fluconazole (300 mg once weekly for 4 weeks) is recommended as the preferred systemic treatment for moderate-to-severe tinea versicolor. Future multicenter studies with longer follow-up are warranted to evaluate long-term recurrence rates.

References

1. *Leong, Cheryl, et al. "Azole resistance mechanisms in pathogenic Malassezia furfur." Antimicrobial agents and chemotherapy 65.5 (2021): 10-1128.*
2. *Sahoo, Alok Kumar, and Rahul Mahajan. "Management of tinea corporis, tinea cruris, and tinea pedis: A comprehensive review." Indian dermatology online journal 7.2 (2016): 77-86.*
3. *Prohic, Asja, et al. "Malassezia species in healthy skin and in dermatological conditions." International journal of dermatology 55.5 (2016): 494-504.*
4. *Sarker, S.K., et al. "Medicine prescribing pattern of dermatology outpatient department in tertiary level hospital at Dhaka City." Journal of Dhaka Medical College 21.1 (2012): 66-68.*
5. *Gaitanis, Georgios, et al. "The Malassezia genus in skin and systemic diseases." Clinical microbiology reviews 25.1 (2012): 106-141.*
6. *Karray, Mehdi, and William P. McKinney. "Tinea versicolor." StatPearls [Internet]. StatPearls Publishing, 2024.*
7. *Rudramurthy, Shivaprakash M., et al. "Association of Malassezia species with dandruff." Indian Journal of Medical Research 139.3 (2014): 431-437.*
8. *Gupta, Aditya K., Kelly A. Foley, and Sarah G. Versteeg. "New antifungal agents and new formulations against dermatophytes." Mycopathologia 182.1 (2017): 127-141.*
9. *Łabędź, Nina, et al. "Pityriasis versicolor—a narrative review on the diagnosis and management." Life 13.10 (2023): 2097.*
10. *Choi, Franchesca D., Margit LW Juhasz, and Natasha Atanaskova Mesinkovska. "Topical ketoconazole: a systematic review of current dermatological applications and future developments." Journal of Dermatological Treatment (2019).*
11. *Howard, Kaitlind C., et al. "A comprehensive overview of the medicinal chemistry of antifungal drugs: perspectives and promise." Chemical Society Reviews 49.8 (2020): 2426-2480.*
12. *Pappas, Peter G., et al. "Clinical practice guideline for the management of candidiasis: 2016 update by the Infectious Diseases Society of America." Clinical infectious diseases 62.4 (2016): e1-e50.*
13. *Begum, Sharmin, et al. "A comparative study of oral Ketoconazole versus Itraconazole in the treatment of Tinea versicolor." Community-Based Medical Journal 9.2 (2020): 26-33.*
14. *Singh, S., et al. "Limited effectiveness of four oral antifungal drugs (fluconazole, griseofulvin, itraconazole and terbinafine) in the current epidemic of altered dermatophytosis in India: results of a randomized pragmatic trial." British Journal of Dermatology 183.5 (2020): 840-846.*
15. *Gupta, Aditya K., and Kelly A. Foley. "Antifungal treatment for pityriasis versicolor." Journal of Fungi 1.1 (2015): 13-29.*
16. *Mirghani, Mohamed. "A review of antifungal activity of combined plant extracts or plant exudates from medicinal plants, either together or with known antifungal agents." European Journal of Medicinal Plants 33.8 (2022): 16-47.*
17. *Melo, Elayne KS, et al. "Criteria for the bioanalytical method and its application in dermatopharmacokinetic (DPK) study in pig skin (ex vivo) using metronidazole." African Journal of Pharmacy and Pharmacology 10.38 (2016): 817-822.*
18. *Sahadevan, Navya Vanaja. "Drug interactions of azole antifungals." Journal of Skin and Sexually Transmitted Diseases 5.1 (2023): 50-54.*

19. *Velegraki, Aristea, et al. "Malassezia infections in humans and animals: pathophysiology, detection, and treatment." PLoS pathogens 11.1 (2015): e1004523.*

20. *US Food and Drug Administration. "FDA Drug Safety Communication: FDA limits usage of Nizoral (ketoconazole) oral tablets due to potentially fatal liver injury and risk of drug interactions and adrenal gland problems." US Food and Drug Administration (2013).*

21. *Chang, Chia-Hsuin, et al. "Severe hepatic injury associated with different statins in patients with chronic liver disease: a nationwide population-based cohort study." Journal of gastroenterology and hepatology 30.1 (2015): 155-162.*

22. *Eicher, L., et al. "A systematic review of factors influencing treatment adherence in chronic inflammatory skin disease–strategies for optimizing treatment outcome." Journal of the European Academy of Dermatology and Venereology 33.12 (2019): 2253-2263.*

23. *Gupta, Pawan, et al. "A Cost Variation Analysis Of Oral And Topical Antifungal Agents Available For The Treatment Of Superficial Fungal Infections In India–An Insight Into The Rising Treatment Cost." Asian J Pharm Clin Res 15.7 (2022): 123-126.*

24. *Sardana, Kabir. Systemic drugs in dermatology. Jaypee Brothers Medical Publishers, 2021.*

25. *Hay, Roderick. "Therapy of skin, hair, and nail fungal infections." Journal of Fungi 4.3 (2018): 99.*