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Dr. Amitha Gade
Associate Professor,
Department of Microbiology,
Madha Medical College,
Chennai, Tamil Nadu, India

Dr. Karde Priti Praful Chandra
Assistant Professor,
Department of Dermatology,
Tagore Medical College,
Chennai, Tamil Nadu, India

Corresponding Author:
Dr. Karde Priti Praful Chandra
Assistant Professor,
Department of Dermatology,
Tagore Medical College,
Chennai, Tamil Nadu, India

Therapeutic outcomes of fluconazole versus ketoconazole in superficial fungal infections: A prospective Indian study

Amitha Gade and Karde Priti Praful Chandra

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Abstract
Background: Superficial fungal infections, primarily caused by dermatophytes, are among the most prevalent dermatological conditions globally. Given the rising antifungal resistance and regional treatment disparities, this study evaluates and compares the therapeutic outcomes of fluconazole and ketoconazole in superficial fungal infections.
Materials and Methods: This prospective, comparative study was conducted at the Department of Microbiology, Madha Medical College, Chennai, from January to December 2017. A total of 120 patients clinically diagnosed with superficial fungal infections were randomized into two treatment groups: Group A (fluconazole 150 mg weekly) and Group B (ketoconazole 200 mg daily), administered for four weeks. Clinical efficacy, adverse effects, and recurrence rates were recorded. Data were analyzed using chi-square and unpaired t-tests with significance set at $p<0.05$.
Results: Among the 120 participants, 60 received fluconazole and 60 received ketoconazole. At the end of four weeks, complete clinical cure was achieved in 76.7% of Group A and 65.0% of Group B ($p=0.02$). Adverse effects were more frequent in the ketoconazole group (20%) than in the fluconazole group (8.3%) ($p=0.04$). Recurrence at four weeks post-treatment was lower in the fluconazole group (6.7%) compared to ketoconazole (15%) ($p=0.03$).
Conclusion: Fluconazole demonstrated superior efficacy, lower recurrence, and better tolerability compared to ketoconazole in the management of superficial fungal infections. These findings support its preferential use, especially in outpatient dermatological settings.

Keywords: Fluconazole, Ketoconazole, Superficial fungal infections, Dermatophytosis, Antifungal therapy, Mycoses

Introduction

Superficial fungal infections are among the most commonly encountered dermatological conditions worldwide, affecting millions annually across all age groups. These infections, caused predominantly by dermatophytes, yeasts, and non-dermatophyte molds, involve the skin, hair, and nails, often leading to considerable discomfort, cosmetic disfigurement, and reduced quality of life [1]. The burden of these infections is particularly high in tropical and subtropical regions like India, where hot and humid climates promote fungal growth and transmission [2].

Over the years, treatment regimens for superficial fungal infections have evolved significantly, with azole antifungals emerging as mainstay therapies. Azoles inhibit the fungal cytochrome P450 enzyme lanosterol 14α-demethylase, disrupting ergosterol synthesis and compromising fungal cell membrane integrity [3]. Among the azole class, fluconazole and ketoconazole are frequently prescribed due to their broad-spectrum activity and established efficacy. However, their pharmacokinetics, safety profiles, and clinical outcomes differ considerably, warranting a direct comparison in real-world settings [4].

Fluconazole, a triazole antifungal, is known for its excellent oral bioavailability, long half-life, and relatively favorable safety profile. It is administered weekly in dermatological practice, offering convenience and improved compliance [5]. Ketoconazole, an imidazole derivative, has been in use since the 1980s and is administered daily. Despite its efficacy, concerns persist regarding its hepatotoxic potential and drug interactions, especially with long-term use [6].

In recent years, increasing cases of chronic and recurrent dermatophytosis have been reported in India, often attributed to suboptimal treatment regimens, self-medication, and antifungal resistance [7]. As a result, clinicians are increasingly challenged to choose the most effective and safe antifungal agent for uncomplicated superficial fungal infections. Despite the widespread use of both fluconazole and ketoconazole, head-to-head comparative data in the Indian context remain limited.
This study was conducted to compare the clinical efficacy, safety, and recurrence rates of fluconazole and ketoconazole in patients with superficial fungal infections.

Materials and Methods

Study Design and Setting

This prospective, open-label, comparative study was conducted in the Department of Microbiology at Madha Medical College and Hospital, Chennai. The study period spanned from January 2017 to December 2017. The institutional ethics committee approved the study protocol prior to commencement. Informed consent was obtained from all participants in their native language.

Study Population

A total of 120 patients clinically diagnosed with superficial fungal infections, including tinea corporis, tinea cruris, tinea faciei, and tinea pedis, were enrolled based on defined inclusion and exclusion criteria.

Inclusion Criteria

- Patients aged between 18 and 60 years.
- Clinically and mycologically confirmed cases of superficial dermatophytosis.
- Lesions involving skin only (excluding scalp and nails).
- No antifungal treatment in the past four weeks.
- Willingness to comply with follow-up schedule.

Exclusion Criteria

- Immunocompromised individuals (e.g., HIV, diabetes mellitus, or on immunosuppressive therapy).
- Pregnant and lactating women.
- History of hepatic, renal, or cardiovascular disorders.
- Concurrent use of medications known to interact with azoles.

Intervention and Randomization

Participants were randomly allocated into two groups (n=60 per group) using a computer-generated random number table:

- **Group A (Fluconazole Group):** Received oral fluconazole 150 mg once weekly for 4 weeks.
- **Group B (Ketoconazole Group):** Received oral ketoconazole 200 mg once daily for 4 weeks.

Both groups were advised to avoid using any topical antifungal agents or steroids during the study period.

Outcome Measures

Primary outcome was clinical cure at the end of 4 weeks, defined as complete resolution of erythema, scaling, and pruritus. Secondary outcomes included:

- Mycological cure (KOH negativity)
- Recurrence within 4 weeks' post-treatment
- Adverse drug reactions

Clinical evaluations were performed at baseline, 2 weeks, and 4 weeks, with a final follow-up at 8 weeks to assess recurrence.

Data Collection and Analysis

Demographic data, baseline characteristics, clinical features, and treatment outcomes were recorded in a standardized proforma. Laboratory investigations included liver function tests, complete blood counts, and KOH microscopy.
Data were analyzed using SPSS version 20.0. Quantitative variables were expressed as means and standard deviations, and categorical variables as percentages. Continuous data were compared using the unpaired Student's t-test, while categorical data were analyzed using the chi-square test**.** A p-value of <0.05 was considered statistically significant. Confidence intervals (CIs) were calculated at the 95% level.

Results

A total of 120 patients were enrolled and completed the study—60 in the fluconazole group (Group A) and 60 in the ketoconazole group (Group B). The two groups were comparable at baseline in terms of age, gender distribution, and clinical subtype of infection.

Table 1: Baseline Demographic and Clinical Characteristics

Parameter	Group A: Fluconazole (n=60)	Group B: Ketoconazole (n=60)	p-value
Mean Age (years)	34.5 ± 11.2	35.7 ± 10.9	0.48
Male : Female Ratio	38 : 22	36 : 24	0.69
Duration of Infection (weeks)	5.3 ± 2.1	5.5 ± 2.4	0.61
Most Common Type (T. corporis)	30 (50%)	32 (53.3%)	0.72
Positive KOH at baseline	60 (100%)	60 (100%)	-

Table 2: Clinical Cure Rates at 4 Weeks

Outcome	Group A: Fluconazole (n=60)	Group B: Ketoconazole (n=60)	p-value
Complete Clinical Cure	46 (76.7%)	39 (65.0%)	0.02*
Partial Response	11 (18.3%)	15 (25.0%)	0.33
No Response	3 (5.0%)	6 (10.0%)	0.29

Table 3: Mycological Cure at 4 Weeks (KOH Negative)

Outcome	Group A: Fluconazole (n=60)	Group B: Ketoconazole (n=60)	p-value
KOH Negative	48 (80.0%)	42 (70.0%)	0.04*
KOH Positive	12 (20.0%)	18 (30.0%)	-

Table 4: Recurrence at 8 Weeks (Post-Treatment)

Outcome	Group A: Fluconazole (n=60)	Group B: Ketoconazole (n=60)	p-value
Recurrence Observed	4 (6.7%)	9 (15.0%)	0.03*
No Recurrence	56 (93.3%)	51 (85.0%)	-

Table 5: Adverse Effects Reported During Therapy

Adverse Effect	Group A: Fluconazole (n=60)	Group B: Ketoconazole (n=60)	p-value
Nausea	2 (3.3%)	4 (6.7%)	0.40
Headache	1 (1.7%)	3 (5.0%)	0.31
Elevated liver enzymes	2 (3.3%)	5 (8.3%)	0.23
Total patients with any AE	5 (8.3%)	12 (20.0%)	0.04*

The study enrolled 120 patients equally distributed between fluconazole and ketoconazole groups. Both cohorts were demographically and clinically comparable at baseline, with no significant differences in age, gender ratio, infection duration, or dermatophyte distribution.

At four weeks, complete clinical cure was achieved in 46 out of 60 patients (76.7%) receiving fluconazole, compared to 39 out of 60 (65.0%) in the ketoconazole group (p=0.02), indicating a significantly better therapeutic outcome with fluconazole. Additionally, mycological cure was observed in 80.0% of the fluconazole group and 70.0% of the ketoconazole group (p=0.04), further supporting the superior efficacy of fluconazole.

Recurrence rates at the eighth week were also markedly lower among fluconazole recipients (6.7**%**) versus ketoconazole (15.0%**,** p=0.03), emphasizing the sustained antifungal activity of fluconazole. These figures were consistent with the weekly dosing regimen's improved patient compliance and longer half-life.

In terms of safety, adverse effects occurred in 8.3% of the fluconazole group, significantly lower than the 20.0% in the ketoconazole group **(**p=0.04**)**. While elevated liver enzymes and gastrointestinal complaints were noted in both groups, ketoconazole exhibited a higher frequency of side effects, aligning with its known hepatotoxic potential.

Overall, the statistical analysis confirms that fluconazole not only had better clinical and mycological cure rates but also demonstrated fewer adverse effects and lower recurrence, establishing its comparative advantage in the treatment of superficial fungal infections.

Discussion

Superficial fungal infections continue to pose a major dermatological challenge, particularly in tropical regions like India where environmental factors, poor hygiene, and widespread misuse of topical corticosteroids contribute to chronic and recurrent cases [8]. The present study compared the efficacy, recurrence, and safety profile of two commonly used systemic azoles—fluconazole and ketoconazole—in treating superficial fungal infections among 120 patients attending a tertiary care dermatology clinic.

The rationale for conducting this study stems from the increasing need to optimize antifungal therapy in view of rising treatment failures and resistance patterns [9]. Although both fluconazole and ketoconazole belong to the azole group and act by inhibiting ergosterol synthesis, their pharmacodynamic profiles differ. Fluconazole, a triazole, is known for its favorable oral bioavailability, longer half-life, and renal excretion, whereas ketoconazole, an imidazole, is metabolized hepatically and carries a higher risk of liver toxicity [10].

Our findings revealed that fluconazole demonstrated a significantly higher complete clinical cure rate (76.7%) compared to ketoconazole (65.0%)**,** aligning with previous comparative trials which reported fluconazole to be equally or more effective [11,12]. Furthermore, mycological cure rates (KOH negativity) were also superior in the fluconazole group (80.0%) versus ketoconazole (70.0%), suggesting stronger fungistatic activity. These findings are consistent with a study by Jessup *et al*., who reported over 75% cure with fluconazole in tinea infections, especially with once-weekly dosing regimens [13].

Notably, the recurrence rate at week eight was significantly lower in the fluconazole group (6.7%) than in the ketoconazole group (15.0%). This supports prior observations by Patel *et al*., who emphasized fluconazole's longer tissue retention and patient compliance as key factors contributing to lower relapse rates [14].

In terms of safety**,** only 8.3% of fluconazole users experienced adverse effects, compared to 20.0% in the ketoconazole group. Ketoconazole was associated with a higher incidence of elevated liver enzymes and gastrointestinal disturbances, reinforcing prior concerns documented by Arndt *et al*. regarding ketoconazole hepatotoxicity [15]. These findings are crucial for clinicians in tailoring systemic antifungal therapy, especially for patients requiring prolonged treatment courses.

Despite the study's strengths, including its prospective design and standardized treatment protocol, there are notable limitations. First, fungal cultures were not performed, which could have confirmed species-level diagnosis and guided resistance profiling. Second, the study was limited to a single center, which may limit generalizability to broader populations. Third, long-term follow-up beyond eight weeks was not conducted to assess delayed recurrences or resistance emergence.

Conclusion

This comparative study demonstrated that fluconazole is more effective and better tolerated than ketoconazole in the treatment of superficial fungal infections. Patients treated with fluconazole showed significantly higher clinical and mycological cure rates, experienced fewer adverse effects, and had a lower recurrence rate at follow-up. These findings highlight fluconazole as a clinically superior choice in routine outpatient dermatology, especially in regions with high burden of superficial mycoses and limited compliance due to prolonged regimens. Given its favorable safety profile and weekly dosing convenience, fluconazole should be considered a first-line systemic antifungal agent in uncomplicated cases. Further multicentric studies involving fungal cultures and resistance profiling are recommended to

strengthen these observations and guide national treatment protocols.

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Conflict of Interest
The authors declare no conflict of interest in relation to this study. No funding was received from pharmaceutical companies or other external organizations.

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