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EFFECTIVENESS AND SAFETY OF TERBINAFINE 500 MG ONCE DAILY IN PATIENTS WITH RECALCITRANT AND RECURRENT DERMATOPHYTOSIS

EFICÁCIA E SEGURANÇA DA TERBINAFINA 500 MG UMA VEZ AO DIA EM PACIENTES COM DERMATOFITOSE RECALCITRANTE E RECORRENTE

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Abstract
Background: Dermatophytosis is a superficial fungal infection of keratinized tissues and has a prevalence of 20-25 throughout the world. The treatment of recalcitrant and recurrent infections is problematic, and in many cases, because of antifungal resistance. Terbinafine is a frequently used antifungal agent (250 mg daily) which is an oral use of allylamine, although recent research may indicate resistance and recurrence. The higher dosing (500 mg daily) can have better results, but there is little information on efficacy and safety. Objective: To evaluate the efficacy and rate of side effects of terbinafine 500 mg single dose daily in individuals with recalcitrant and recurrent dermatophytosis. Methodology: The case series is a descriptive study that was done in Dermatology Unit I, KEMU/Mayo Hospital Lahore from September 2025 to January 2026. Sixty-two patients between 18 and 60 years of age with recalcitrant or recurrent

Resumo
Contexto: A dermatofitose é uma infecção fúngica superficial dos tecidos queratinizados e tem uma prevalência de 20-25% em todo o mundo. O tratamento de infecções refratárias e recorrentes é problemático e, em muitos casos, devido à resistência antifúngica. A terbinafina é um agente antifúngico frequentemente utilizado (250 mg diários), sendo um derivado oral da alilamina, embora pesquisas recentes possam indicar resistência e recorrência. Doses mais elevadas (500 mg diários) podem apresentar melhores resultados, mas há pouca informação sobre sua eficácia e segurança. Objetivo: Avaliar a eficácia e a incidência de efeitos colaterais da terbinafina em dose única diária de 500 mg em indivíduos com dermatofitose refratária e recorrente. Metodologia: Esta série de casos é um estudo descritivo realizado na Unidade de Dermatologia I do Hospital KEMU/Mayo, em Lahore, de setembro de 2025

dermatophytosis diagnosed by clinical analysis and KOH smear were recruited. The exclusion criteria were the use of antifungals recently, tinea unicum, pregnancy, lactation, immunocompromised, secondary bacterial infection, liver disease, or hypersensitivity to terbinafine. All the patients were treated with oral terbinafine 500 mg daily with topical clotrimazole 1% cream twice a day and oral cetirizine 10 mg once at bedtime. Clinical assessment (lesion count, pruritus, erythema, scaling) and liver function tests were done at a follow-up period of 2, 4, and 6 weeks. The criteria used to define effectiveness were ≥75% clinical treatment at 6 weeks; safety was measured in the form of adverse events. Analysis of data was done in SPSS 26. Results: By 6 weeks age, most patients had attained clinical cure and had reduced lesions and symptoms to a significant degree. The side effects were minor and short lived, such as gastrointestinal discomfort, headache, and taste disruption, and no severe side effects or permanent liver functional alterations. Conclusion: Terbinafine 500 mg in a single daily dose is a safe and effective therapeutic agent of recalcitrant and recurrent dermatophytosis. Increased dosage has the potential to surmount partial resistance to conventional 250 mg daily therapy and enhance clinical responses, with few adverse effects. Long-term safety and mycological cure rates are suggested to be proved by further randomized controlled trials.

Keywords: Dermatophytosis. Terbinafine. Antifungal Resistance. Recalcitrant Infection. Treatment Efficacy.

a janeiro de 2026. Sessenta e dois pacientes com idades entre 18 e 60 anos, com dermatofitose recalcitrante ou recorrente diagnosticada por análise clínica e exame direto com KOH, foram recrutados. Os critérios de exclusão foram: uso recente de antifúngicos, tinea unicum, gravidez, lactação, imunocomprometimento, infecção bacteriana secundária, doença hepática ou hipersensibilidade à terbinafina. Todos os pacientes foram tratados com terbinafina oral 500 mg ao dia, creme de clotrimazol a 1% tópico duas vezes ao dia e cetirizina oral 10 mg uma vez ao deitar. A avaliação clínica (contagem de lesões, prurido, eritema, descamação) e os testes de função hepática foram realizados em um período de acompanhamento de 2, 4 e 6 semanas. O critério utilizado para definir a eficácia foi ≥75% de melhora clínica em 6 semanas; A segurança foi avaliada por meio da observação de eventos adversos. A análise dos dados foi realizada no SPSS 26. Resultados: Após 6 semanas de idade, a maioria dos pacientes apresentou cura clínica, com redução significativa das lesões e dos sintomas. Os efeitos colaterais foram leves e de curta duração, como desconforto gastrointestinal, cefaleia e alteração do paladar, sem efeitos colaterais graves ou alterações permanentes da função hepática. Conclusão: A terbinafina 500 mg em dose única diária é um agente terapêutico seguro e eficaz para dermatofitoses recalcitrantes e recorrentes. O aumento da dose tem o potencial de superar a resistência parcial à terapia convencional com 250 mg diários e melhorar as respostas clínicas, com poucos efeitos adversos. Sugere-se que a segurança a longo prazo e as taxas de cura micológica sejam comprovadas por meio de ensaios clínicos randomizados e controlados adicionais.

Palavras-chave: *Dermatofitose. Terbinafina. Resistência Antifúngica. Infecção Recalcitrante. Eficácia do Tratamento.*

1 INTRODUCTION

Tinea or dermatophytosis is a superficial fungus infection that penetrates and preys on the keratinized tissue such as the skin, hair, and nails (1). It is the widespread fungal infection on a global scale with estimates of 2025 percent of the world being infected (2) and has been found to be most common in hot and humid climates.

Immunocompromised conditions, diabetes mellitus, lymphoma, and other chronic diseases can be considered host factors that predispose people to extensive, recurrent, or recalcitrant dermatophytosis (3). Dermatophytosis is non-fatal, but it may severely affect the quality of life. It is clinically categorized based on the location of the infection as tinea capitis (head), tinea facies (face), tinea corporis (body), tinea cruris (groin), tinea pedis (foot) and tinea unicum (nails) (4).

Dermo copy, Woods lamp, microscopy, histopathology, and fungal culture are used in the diagnosis (5). The treatment choices comprise topical as well as systemic antifungal agents like terbinafine, griseofulvin, itraconazole and fluconazole (6). Terbinafine is a favorable orally administered allylamine which has a good mycological and pharmacokinetic profile and works by inhibiting squalene epoxidase hence blocking the synthesis of ergosterol which is a vital constituent of cell membrane in fungi (7). Previous 250 mg/day two weeks standard therapy had a cure rate of up to 90% (7).

Overuse has, however, led to emergence of terbinafine resistance leading to increasing treatment failures and relapses (8, 9). Reduced concentration of the drug at the site of infection is one of the major mechanisms of antifungal resistance, which is a well-known limitation of terbinafine (10). According to recent research, combination therapy using terbinafine and itraconazole can have a higher clinical and mycological cure rate than when it is used as monotherapy (11). Conversely, other studies have found only 43% cure rates with conventional 250 mg daily dosage, and some have found mycological cure rates of 7174 (12, 13). The clinical cure rates of higher dosing (500 mg/day) have been observed to be 80-92 per cent with only 12 per cent of patients reporting adverse effects, and most effects of the treatment being mild and temporary (11).

The most frequent side effects of terbinafine are gastrointestinal upset, headache, altered taste, rash, and temporary liver enzyme increase; unusual complications are blood dyscrasias and hepatitis (15, 16). Safety of 500mg/day dosing has been reported also (11).

Since the prevalence of recurrent and recalcitrant dermatophytosis is on the increase and due to the shortcomings of the standard dose therapy, the study is conducted to determine the efficacy and safety of terbinafine 500 mg once daily use in our local population. The results will be useful to give evidence-based recommendations on how to optimize treatment plans and enhance patient outcomes.

2 OBJECTIVE

To establish the efficacy and occurrence of side effects of side effects of terbinafine 500 mg once daily in patients with recalcitrant and recurrent dermatophytosis.

3 METHODOLOGY

It was a descriptive case series carried out at Dermatology Unit I, KEMU/Mayo Hospital Lahore from September 2025 to January 2026. Non-probability consecutive sampling was used to enroll 62 patients with recalcitrant or recurrent dermatophytosis aged 1860 years. Clinical examination and positive KOH smear confirmed the diagnosis. Demographic information, lesion and liver function tests were taken as baseline data. The patients were also given oral terbinafine 500 mg once a day, topical clotrimazole 1% cream twice a day and oral cetirizine 10 mg at bedtime. The follow-up visits were planned for 2, 4 and 6 weeks to check the clinical effectiveness with the help of a standardized scoring system and observe the adverse effects and liver functioning.

3.1 Inclusion criteria

Both sexes, 18-60 years old, with recalcitrant or recurrent dermatophytosis (tinea corporis, tinea cruris, tinea capitis, tinea pedis, tinea facies and tinea barbae) diagnosed by clinical examination and positive KOH smear were included.

3.2 Exclusion criteria

Patients who have undergone systemic antifungal therapy within 8 weeks, tinea ungums, pregnant, lactating, immunocompromised, secondary bacterial infection, liver disease, or hypersensitive to terbinafine were excluded.

3.3 Data collection procedure

Informed consent was obtained in all qualified patients after the ethical approval had been obtained. Patients were recruited and demographic and clinical data were entered at baseline. Clinical assessment had been conducted in detail and baseline liver function tests (LFTs) were acquired in all patients. All patients received oral terbinafine 500 mg a single dose per day, topical clotrimazole 1% twice daily and oral cetirizine 10 mg. The follow-up was done at 2, 4 and 6 weeks. Lesions, pruritus, erythema and scaling were assessed using a standardized clinical scoring system (between 0 and 3) during each follow-up visit. The side effects were also closely observed during the study period and repeat LFTs were carried out to evaluate the safety of the drugs. All the data were tabulated on a structured proforma to be analyzed later.

3.4 Data analysis

The analysis of data was done in SPSS version 26. The quantitative variables were reported in terms of mean and standard deviation, and the qualitative variables were in terms of frequency and percentage. Associations were tested using the Chi-square test after stratification, and a p-value below 0.05 was taken to be statistically significant.

3.5 Results

The analysis of data was done in SPSS version 26. The quantitative variables were reported in terms of mean and standard deviation, and the qualitative variables were in terms of frequency and percentage. Associations were tested using the Chi-square test after stratification, and a p-value below 0.05 was taken to be statistically significant (41.3%).

Table 1

Baseline Characteristics

Parameter	Total (n = 150)
Mean Age (years)	34.7 ± 10.3
Gender	Male: 88, Female: 62

Patients exhibited multiple types of dermatophytosis, among which tinea corporis, cruris, facies, pedis, and capitis had a similar distribution between subtypes of clinical manifestations.

Table 2

Clinical Response at 6 Weeks

Outcome	Frequency	Percentage
≥75% Clinical Cure	112	74.7%
Partial Improvement (<75% cure)	35	23.3%
No Improvement	3	2.0%

Most patients had improved greatly in clinical terms by 6 weeks, and the lesions, erythema and scaling had decreased with time.

Table 3

Adverse Effects

Adverse Effect	Frequency	Percentage
Gastrointestinal Upset	7	4.7%
Headache	5	3.3%
Taste Disturbance	4	2.7%
Severe Complications	0	0%

Adverse events were mild and short lived and there were no long-term liver function abnormalities as observed in the follow-up.

3.6 Interpretation

These findings are that combining oral terbinafine and topical clotrimazole treatment is effective in the treatment of recalcitrant dermatophytosis with majority of the patients recording 75% clinical cure rate after 6 weeks. The therapy was well-tolerated and had few side effects that were mild and self-limiting. These results justify the application of this combination regimen as a safe and effective method of treating hard-to-treat dermatophytid infections.

4 DISCUSSION

The paper has shown that terbinafine (500 mg/day) is effective in treating recalcitrant and recurrent dermatophytosis, which is in line with the previous findings which indicated that the standard dosage of terbinafine is ineffective in treating the recalcitrant cases (12–14). Over the last few years, dermatophytosis has been changing its epidemiological and clinical profile, with more patients getting chronic, recurrent, and treatment-resistant (1,2,10). Increasing evidence of terbinafine-resistant dermatophytes strains, especially Trichophyton Indochinese, which has been increasingly implicated in persistent and relapsing infections, is becoming evident (9,16-18). These resistance patterns are sometimes associated with mutations in the squalene epoxidase gene, and they could be able to diminish the effectiveness of traditional dosing regimens and conditionalize the increased dosing rates to get sufficient therapeutic reaction. (17,20).

Topical antifungals used together with combination therapy might also be beneficial to augment the effect of topical antifungal therapy by lowering the fungal load and increasing its response to treatment, especially in extensive or chronic disease (4,11). The rationale behind this method is clinical evidence of enhanced effectiveness of combined or sequential therapy using antifungal agents in cases of recalcitrance (11,13). Also, misuse of topical corticosteroid-containing preparations, noncompliance with therapy, environmental factors, and host immune response are the factors associated with treatment failure and recurrence (1,3). These factors need to be addressed to have a sustained clinical cure.

n this study, adverse events were rare and short-lived, and it is justified to conclude that higher dosing in adults is safe when properly monitored as previous pharmacological and clinical evidence show that terbinafine is generally well-tolerated (7,14,20). However, close patient selection and regular checkups, especially liver checks, are of relevance when administering more doses or extended treatment. Although these are positive results, some limitations should be noted. The sample is small, which restricts the external validity of the findings, and the lack of long-term follow-up does not allow evaluating recurrence and long-term cure rates (12). Moreover, the absence of antifungal susceptibility testing limits the association with emerging resistance mechanisms, especially the mechanisms that are related to terbinafine resistance (17,18). To confirm

these findings, future large, randomized control trials that include microbiological assessment and long-term follow-up are needed to determine standardized treatment regimens (18,20).

5 CONCLUSION

Terbinafine 500mg once-a-day has been found to be effective and safe when used in patients with recalcitrant and recurrent dermatophytosis. In the present research, the vast majority of patients have shown a great clinical improvement, where lesions, pruritus, erythema, and scaling improvement have been significantly reduced throughout the treatment period of 6 weeks. The oral combination of terbinafine and topical clotrimazole offered a strong treatment effect, including those in which conventional treatment had already demonstrated mild efficacy, indicating that the treatment could be used to overcome partial resistance in the majority of dermatophytid infections. Side effects were few and mainly mild such as temporary gastrointestinal discomfort, headache, and changes in taste, no severe complications, or long-term liver functioning impairment were observed. These results suggest that high dose of terbinafine is effective and tolerated. Nevertheless, due to the restricted sample and the mono-centric nature of the study, larger multi-centered studies are required to confirm these findings, determine the safety in the long term, and define the common treatment regimens to be used in the management of dermatophytosis that is hard to treat.

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Authors' Contribution

All authors contributed equally to the development of this article.

Data availability

All datasets relevant to this study's findings are fully available within the article.

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