Dermatology Practical & Conceptual

Retrospective Cohort Study of Hepatic and Hematologic Toxicity in Terbinafine-Treated Onychomycosis Patients With Reduced Kidney Function at an Academic Institution

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Introduction

Oral terbinafine, a first-line onychomycosis therapy, is primarily excreted renally [1, 2]. Patients with renal impairment may have increased hepatic and hematologic toxicity risk. Onychomycosis was ~2x more common in hemodialysis and kidney transplant patients vs. non-renal disease controls in a prospective study (N=510, *P*=0.03) [3]. Therefore, we aimed to evaluate the association between kidney function and laboratory test abnormality rates in terbinafine-treated onychomycosis patients.

Case Presentation

Aspartate aminotransferase (AST), alanine aminotransferase (ALT), and complete blood count (CBC) tests of terbinafine-treated adults with onychomycosis (2000-2021) ≤3 months before, during, and ≤3 months after treatment were collected (Supplemental Methods).

Of 2,195 records, 734 patients were included, with an average age of 55.2 years (Supplemental Table 1). Two hundred eighty-five patients had abnormal renal function, and proportion of abnormal AST, ALT, and CBC values

were similar during and post-terbinafine treatment vs. pre-treatment (Supplemental Table 2). After matching for age, sex, weight, hepatic/hematologic disease, terbinafine-treated stage 2 chronic renal insufficiency (CRI) vs. stage 1 CRI and stage 3 CRI vs. stage 1 CRI patients had similar laboratory abnormality risk during and post-treatment vs. baseline (Table 1). Stage 1 CRI patients had mean 0.02mg/dL serum creatinine change from baseline to during treatment and baseline to post-treatment (both 95% CI: 0.01–0.04, *P*=0.002, *P*=0.005, respectively). Mean creatinine was stable from baseline to during and post-treatment for stages 2 and 3 CRI (Supplemental Table 3).

Discussion

Our study suggests that terbinafine-treated onychomycosis patients with stages 2 or 3 CRI are not at increased risk of developing laboratory abnormalities vs. patients with normal kidney function (stage 1 CRI). Creatinine increased in stage 1 CRI terbinafine-treated patients, which may be due to laboratory variations and was clinically insignificant.

We found no difference between baseline and monitoring hepatic and hematologic laboratory values, similar to a retrospective cohort study [4] of 4,309 terbinafine courses for dermatophyte infection (majority onychomycosis), where transaminitis, anemia, lymphopenia, and neutropenia rates were low and comparable to baseline. In a population-based study [5] of 12,376 patients, incidence of terbinafine-induced liver injury was 1.6/10,000 persons.

Since terbinafine is primarily excreted in the urine (80%), with creatinine clearance decreased by 50% in patients with <50 mL/min [1], reducing daily terbinafine dosage by half has been suggested for patients with reduced renal function [2]. However, the package insert does not mention dose reduction

Table 1. Risk of developing laboratory abnormalities in terbinafine-treated patients with Stage 2/ Stage 3 CRI compared to patients with stage 1 CRI*

Stage 2 CRI compared to stage 1 CRI			
Outcome variable	**Odds ratio**	**95% confidence interval**	***P* value**
Abnormal AST results post-treatment	1.21	0–785.34	0.131
Abnormal AST results during treatment	0.85	0.36–2.02	0.717
Abnormal ALT results post-treatment	0.29	0.06–1.48	0.137
Abnormal ALT results during treatment	0.98	0–644.37	0.994
Abnormal CBC results post-treatment	1.01	0.4–2.55	0.981
Abnormal CBC results during treatment	1.49	0.67–3.3	0.329
Stage 3 CRI compared to stage 1 CRI			
Outcome variable	**Odds ratio**	**95% confidence interval**	***P* value**
Abnormal AST results post-treatment**	--	--	--
Abnormal AST results during treatment	0.9	0.11–7.17	0.924
Abnormal ALT results post-treatment**	--	--	--
Abnormal ALT results during treatment**	--	--	--
Abnormal CBC results post-treatment	3.66	0.5–26.79	0.202
Abnormal CBC results during treatment	3.35	0.54–20.82	0.194

*After matching and adjusting for covariates, including age, sex, weight, presence of hepatic/hematologic disease, and baseline AST, ALT, CBC laboratory tests.
**Odds ratios could not be calculated due to lack of laboratory values in stage 1 or stage 3 groups.
Abbreviations: ALT: alanine aminotransferase; AST: aspartate aminotransferase; CBC: complete blood count; CRI: chronic renal insufficiency.

in renally impaired patients [1], with a paucity of studies to support this recommendation. In a retrospective study of 13 kidney transplant recipients (creatinine <3.39 mg/dL) treated with terbinafine (250 mg daily, 12 weeks) for onychomycosis, none had hepatic or hematologic abnormalities, suggesting that terbinafine may be safe even in patients with severely reduced kidney function [4].

Limitations include small sample size, confounding bias, single-center design, and lack of consideration of dosage and adverse event-related treatment interruptions. Few patients had severe renal impairment.

Conclusions

In sum, onychomycosis patients with mild to moderate reduced kidney function do not seem to have increased risk of developing laboratory abnormalities with terbinafine treatment, and dose reduction may not be necessary. We recommend checking baseline creatinine to evaluate renal function before prescribing terbinafine for onychomycosis treatment, pending larger multicenter trials evaluating onychomycosis patients with kidney disease.

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