Medicine by the Numbers

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Terbinafine for Onychomycosis

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Details for This Review

Study Population: Patients 36 to 68 years of age with toenail onychomycosis confirmed by positive culture or fungal elements noted on microscopy

Efficacy End Points: Cure of toenail onychomycosis by clinical appearance and microscopic evaluation; time to cure and recurrence rate also monitored

Harm End Points: Adverse events associated with medication (headaches, dyspepsia, nausea, rash, taste disorders, viral infection, fatigue, hepatotoxicity, medication interactions)

TERBINAFINE (LAMISIL) FOR ONYCHOMYCOSIS

Benefits	Harms
1 in 3 treated were clinically cured when compared with those receiving placebo	None were harmed
1 in 3 treated were clinically cured when compared with griseofulvin	
1 in 10 treated were clinically cured when compared with azoles	
1 in 7 treated with terbinafine plus an azole were clinically cured when compared with terbinafine alone	

Narrative: Toenail onychomycosis is reported to have a prevalence of 2% to 14% in the Western adult population. It is a common presenting condition in most primary care clinics.[1] Although onychomycosis can be painful, patients most often present for cosmetic concerns associated with nail appearance. Treatment is important, especially in older adults and patients with diabetes mellitus because onychomycosis can lead to cellulitis and foot ulcers in these populations. Oral medications are the preferred treatment for onychomycosis given increased rates of cure over topical medications.[2]

A recent Cochrane review was published comparing terbinafine (Lamisil) to other antifungal medications for treatment of onychomycosis.[3] This review evaluated 48 randomized controlled trials based in Western countries and involved 10,200 participants, comparing terbinafine vs. placebo, terbinafine vs. azoles, terbinafine vs. griseofulvin, and terbinafine plus an azole vs. terbinafine alone. Terbinafine was found to be effective for treatment compared with placebo (relative risk [RR] = 6.0; 95% confidence interval [CI], 3.96 to 9.08). Terbinafine was also found to be more effective than azoles for clinical cure (RR = 0.82; 95% CI, 0.72 to 0.95). Terbinafine and azoles were found to have the same rate of adverse events. Terbinafine was more effective than griseofulvin (RR = 0.32; 95% CI, 0.14 to 0.72). Griseofulvin was also found to have a higher rate of adverse events than terbinafine (RR = 2.09; 95% CI, 1.15 to 3.82). When combined with an azole, terbinafine was found to be more effective than terbinafine alone (RR = 1.41; 95% CI, 0.01 to 1.97). The terbinafine and azole combination did not have a statistically increased incidence of adverse events (RR = 0.64; 95% CI, 0.34 to 1.21).[3]

Caveats: This meta-analysis compared rates of clinical and mycologic cure. In the literature, clinical cure is typically reported as 80% to 100% normal appearing nail following treatment.[4] This is a subjective measure that is difficult to standardize across studies. Values reported in this review are isolated to the clinical cure rate to reflect the general clinical practice of basing treatment completion on clinical cure and not repeat mycologic evaluation.

The NNT Group Rating System

Green	Benefits greater than harms
Yellow	Unclear benefits
Red	No benefits
Black	Harms greater than benefits

Terbinafine has been associated with increased risk of hepatic injury and hepatotoxicity. Baseline and periodic liver function tests are recommended while administering this medication.[2] The risk of adverse events between terbinafine and placebo was found to be nonstatistically significant (RR = 1.13; 95% CI, 0.87 to 1.47).[3] It is unclear if the actual risk of adverse events is more pronounced outside of these well-designed clinical trials. The recommended treatment course for terbinafine is six weeks for fingernail infections and 12 weeks for toenail infections.[2]

Preliminary evidence indicates that combining terbinafine with an azole appears to be superior to terbinafine alone. This is based on low-quality evidence, including one study with only 176 participants.[3] No available data have compared combination treatment with placebo. Further study is necessary to compare combined treatment with terbinafine plus an azole vs. terbinafine alone.

This series is coordinated by Dean A. Seehusen, MD, MPH, *AFP* Assistant Medical Editor, and Daniel Runde, MD, from the NNT Group.

A collection of Medicine by the Numbers published in *AFP* is available at https://www.aafp.org/afp/mbtn.

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