Oral Treatment of Onychomycosis

Epstein E. How often does oral treatment of toenail onychomycosis produce a disease-free nail? An analysis of published data. Arch Dermatol 1998; 134:1551-4.

Clinical question **How effective are the newer oral antifungals for the treatment of toenail onychomycosis?**

Background Standard topical antifungals are ineffective for the treatment of onychomycosis, and treatment with griseofulvin and ketoconazole is hampered by low cure rates, high relapse rates, high incidence of side effects, and the need for lengthy dosing schedules.[1] Newer oral agents such as itraconazole, terbinafine, and fluconazole have more favorable side-effect profiles and shorter dosing schedules. Although previous studies using these agents have reported high cure rates, there had been no recent systematic review to determine the relative efficacy of these agents in curing and preventing relapse of toenail onychomycosis.

Population studied This review included only studies enrolling 15 or more subjects with isolated toenail onychomycosis.

Study design and validity This is a systematic review rather than a meta-analysis, because it falls short of statistically combining data into a single estimate of efficacy. Studies from the MEDLINE database were identified using a title search for the key word "toenail," and medical subject heading searches combining "onychomycosis" and "therapy." Of these, only studies that used both clinical (morphologic) and mycologic (potassium hydroxide preparation and culture) cure as an end point were included in the analysis. The frequency with which treatment achieved disease-free nails was calculated for each study. Unfortunately, no study of fluconazole met the inclusion criteria for this review.

Outcomes measured The primary outcomes were the frequency of attaining a disease-free nail 1 year after the start of treatment and the relapse rate at 2 years. The former could be calculated for 3 studies of itraconazole and 8 studies of terbinafine. The 2-year relapse rate was calculated for 1 study of itraconazole; terbinafine studies lacked the data to allow relapse-rate calculation.

Results Except for 1 small study, the disease-free nail rates after 1 year of treatment were from 38% to 52% for terbinafine. Disease-free nail rates for itraconazole were 33% to 35%. The relapse rate in the 1 study of itraconazole was 17% at 2 years. No studies of terbinafine reported a relapse rate, and no studies of any oral agent reported relapse rates beyond 2 years.

A common weakness of the reviewed studies was the practice of considering "improved nail morphology" or a "90% to 100%" normal nail as a successful outcome without requiring complete mycologic and morphologic cure. Other limitations included assessing a target nail to gauge cure rather than assessing all diseased nails, reporting relapse figures without supporting data, and estimating relapse by gross morphologic findings without mycologic findings.

Recommendations for clinical practice **The cure rate for toenail onychomycosis appears to be higher with terbinafine than with itraconazole, and cure rates for either agent exceed those reported in most trials of griseofulvin.[1] However, given the lack of long-term relapse data and the flawed assessment of cure that characterized many of these studies, as well as the treatment's high cost and low clinical efficacy, we do not recommend the widespread use of these drugs. Until a well-designed randomized controlled clinical trial establishes improved and lasting efficacy of 1 or more of the oral agents, their use should be considered only on a case-by-case basis.**

Mark R. Ellis, MD, MSPH
Kevin Y. Kane, MD
University of Missouri–Columbia
E-mail: ellismr@health.missouri.edu

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Prophylactic Mastectomy for Prevention of Breast Cancer

Hartmann LC, Schaid DJ, Woods JE, et al. Efficacy of bilateral prophylactic mastectomy in women with a family history of breast cancer. N Engl J Med 1999; 340:77-84.

Clinical question **Does bilateral prophylactic mastectomy prevent breast cancer in women with a family history of breast cancer?**

Background Breast cancer is the most common cancer in American women and will affect 1 in 9 in their lifetime.[1] Family history and genetic analysis can be used to predict individual risk levels. Women at high risk can be offered careful surveillance, chemopreventive therapy, or bilateral prophylactic mastectomy (BPM). The outcome data for women undergoing BPM are incomplete.

Population studied All women with a family history of breast cancer who underwent BPM at the Mayo clinic between 1960 and 1993 were included in the study. The median age at mastectomy was 42 years.

Study design and validity This was a retro-

spective study looking at the incidence of breast cancer and related deaths in women who underwent prophylactic mastectomy. Women who had undergone BPM were divided into moderate- and high-risk groups on the basis of their family history. The Gail model,[2] that considers characteristics such as family history, birth history, and previous breast pathology, was used to calculate the expected incidence of breast cancer in the moderate-risk group as a theoretical control group. The high-risk group was compared with a control group of 403 of their sisters who had not undergone prophylactic mastectomy.

Outcomes measured The primary outcomes were the incidence rates of breast cancer and death from breast cancer.

Results Of the 639 women studied, 214 were classified as high risk and 425 as moderate risk. The median length of follow-up was 14 years. BPM reduced the expected number of breast cancers during the follow-up period among the 214 high-risk women from 37.4 to 3 (number needed to treat [NNT] = 6.2), and the number of deaths from breast cancer from 10.5 to 2 (NNT = 25.2). For the 425 moderate-risk women, the expected number of breast cancers was reduced from 37.4 to 4 (NNT = 12.7), and the number of deaths from breast cancer from 10.4 to 0 (NNT = 39.6).

Recommendations for clinical practice **This study convincingly demonstrates that BPM reduces breast cancer and related deaths in moderate- and high-risk women. It also demonstrates that to prevent cancers in a few women, many other women will undergo unnecessary bilateral mastectomy. In this study, 639 women were treated to prevent 18 cancer deaths. Women need accurate information to calculate their risk of getting breast cancer. They will then be able to weigh the risk of unnecessary surgery—along with emotional factors, such as the fear of breast cancer and the cosmetic impact of mastectomy—against possible prevention in making their decisions. BPM may become a more useful option as the accuracy of predicting the risk of breast cancer improves.**

Laurel M. Kuehl, MD
Sharon Dobie, MCP, MD
University of Washington
Seattle
E-mail: lkuehl@u.washington.edu

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Once-Daily Amoxicillin for Streptococcal Pharyngitis in Children

Feder HM Jr, Gerber MA, Randolph MF, Stelmach PS, Kaplan EL. Once-daily therapy for streptococcal pharyngitis with amoxicillin. Pediatrics 1999; 103:47-51.

Clinical question **Is once-daily therapy with amoxicillin an effective treatment for children with streptococcal pharyngitis?**

Background Group A beta-hemolytic streptococcus (GABHS) pharyngitis remains a fairly common problem for family physicians. Although twice-daily dosing is acceptable in adults, the standard dosing schedule for the pediatric population is 4 times a day.[1] Once-daily dosing would be easier, and might lead to better compliance. The Food and Drug Administration has approved cefadroxil, cefixime, ceftibuten, and azithromycin for once-daily dosing in the treatment of GABHS pharyngitis. However, these antibiotics are much more expensive than penicillin V. Previous trials of once-daily penicillin have produced mixed results. A study published in 1993 showed the effectiveness of once-daily amoxicillin.[2] This study compares once-daily amoxicillin to penicillin V taken 3 times a day.

Population studied The population studied was children with an age range of 4 to 18 years (mean = 9.9) with suspected GABHS pharyngitis in a private pediatric practice.

Study design and validity Consecutive patients with suspected GABHS pharyngitis were considered for the study. Their throats were swabbed for both a rapid antigen test and culture, and they were randomly assigned to a 10-day course of either 750 mg amoxicillin once per day or 250 mg penicillin V 3 times per day. Patients were asked to return for follow-up at 18 to 24 hours, 4 to 6 days, and 14 to 21 days. Clinical symptoms were recorded and throat cultures performed at each follow-up visit. All cultures were performed at the same laboratory, and all GABHS isolates were serotyped (M typing and T agglutination patterns). Patients treated with amoxicillin who had a positive culture at any follow-up visit were then treated with penicillin. Compliance with antibiotics was measured by an assay for urinary antimicrobial activity. Treatment failure was defined as presence of the same serotype of GABHS on a follow-up culture as on the initial culture. Exclusionary criteria included any antibiotic therapy in the week before the visit for pharyngitis and hypersensitivity to penicillin or amoxicillin. This study is methodologically sound but does not have sufficient numbers to examine the rate of suppurative (ie, peritonsillar abscess) or nonsuppurative (ie, poststreptococcal