

# Review: Oral antifungal drugs promote cure of fungal foot infections

Bell-Syer SE, Hart R, Crawford F, et al. **Oral treatments for fungal infections of the skin of the foot.** *Cochrane Database Syst Rev.* 2002;(2):CD003584 (latest version 5 Dec 2001).

## QUESTION

In patients with fungal infections of the skin of the foot (tinea pedis), how effective is oral treatment for eradicating the infection?

## DATA SOURCES

Studies were identified by searching MEDLINE (1966 to 2000), CINAHL (to 2000), SCI and SSCI (1969 to 2000), EMBASE/Excerpta Medica (1980 to 2000), the Cochrane Controlled Trials Register, CAB-Health (1973 to 1997), HealthSTAR (1975 to 1997); hand searching podiatry journals; reviewing bibliographies of reviews; and by contacting pharmaceutical companies and podiatry schools.

## STUDY SELECTION

Studies were selected if they were randomized controlled trials evaluating oral treatment in patients with clinically diagnosed and microscopy and laboratory-confirmed tinea pedis.

## DATA EXTRACTION

2 reviewers independently extracted data on study design, condition, intervention, patient

characteristics, study quality, and outcomes. The main outcome measure was mycological cure (negative results on microscopy and no dermatophyte growth in culture). Secondary outcomes were such clinical signs as redness, scaling, pustules, itching, burning, soreness; recurrence of the condition after achieving cure; and side effects.

## MAIN RESULTS

12 trials were included and evaluated 5 antifungal treatments. 2 trials (1 of terbinafine and 1 of itraconazole) were placebo-controlled; 9 trials compared different oral drugs (terbinafine, itraconazole, ketoconazole, fluconazole, and griseofulvin); and 1 trial compared different doses of fluconazole. Both active drugs were more effective than placebo: terbinafine, 250 mg/d for 6 weeks, had a 65% (95% CI 45 to 86) absolute benefit increase (ABI) 2 weeks after the end of treatment. Itraconazole, 400 mg/d for 1 week had an ABI of 47% (CI 29 to 67) 8 weeks after the end of treatment. Among the 9 trials comparing different drugs, terbinafine was no better than itraconazole in 3 trials, but 1 trial showed a benefit in favor of terbinafine

(ABI 32%, CI 16 to 47); itraconazole (1 trial) and ketoconazole (1 trial) did not differ from fluconazole; and griseofulvin did not differ from ketoconazole (1 trial). 2 trials comparing griseofulvin, 500 mg/d, with terbinafine, 250 mg/d, for 4 or 6 weeks showed a higher cure rate with terbinafine (pooled ABI 52%, CI 33 to 71). 1 trial comparing fluconazole at 50 mg/d for 6 weeks with 150 mg/wk for 6 weeks showed no difference in cure rates. All trials reported short-term side effects, including diarrhea and nausea (most common); headache; and rash, dermatitis, and pruritus.

## CONCLUSION

In patients with fungal infections of the skin of the foot, terbinafine or itraconazole eradicates infection better than placebo, and terbinafine is better than griseofulvin.

*Sources of funding: Wales Office for Research and Development for Health and Social Care and University of York.*

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## COMMENTARY

Tinea pedis (athlete's foot) is an exceedingly common ailment that increases with age and for which men have a clear predilection. The condition is most commonly treated topically with either prescription or nonprescription antifungal agents administered as a cream, ointment, powder, or spray. However, systemic oral therapy of tinea pedis is also effective and is the subject of this Cochrane Review by Bell-Syer and colleagues.

Not surprisingly, oral antifungal treatment was better than placebo, and terbinafine was more effective than griseofulvin. No statistically significant differences were seen between terbinafine and itraconazole in 3 of 4 trials, whereas 1 trial showed an advantage of terbinafine, which is consistent with its superiority over itraconazole in the treatment of toenail onychomycosis (1), a condition attributable to essentially the same fungal pathogens as tinea pedis. The data regarding fluconazole and ketoconazole were more limited, although it should be noted that ketoconazole is rarely used because of concerns about hepatotoxicity and poor bioavailability.

Although not the purpose of the review, the authors did not address the relative efficacy and patient acceptability of oral or topical therapy for tinea pedis, an issue of concern to clinicians. Consequently, clinicians are left on their own in deciding between oral or topical therapy. Furthermore, the optimal duration of therapy for oral treatment of tinea pedis is not clear from the available literature, and it is unlikely that a pharmaceutical sponsor would invest money in determining the shortest duration of therapy. However, when oral therapy is considered, either terbinafine or itraconazole is effective, but the terbinafine regimen has a lower pill burden (1 vs 4 per d) and has fewer drug interactions, making it a somewhat simpler therapy.

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## Reference

1. Evans EG, Sigurgeirsson B. Double-blind, randomised study of continuous terbinafine compared with intermittent itraconazole in treatment of toenail onychomycosis. *BMJ.* 1999;318:1031-5.