Putting the FUN in Fungi: Toenail onychomycosis treatments

Clinical Question: How effective are treatments for mild-moderate adult toenail onychomycosis?

Bottom Line: Up to 45-60% of patients on oral treatments (terbinafine best), 6-23% on topicals (efinaconazole best), and <10% on placebo will be “cured” after ~1 year. Topicals should be reserved for cases with minimal (<40%) nail involvement.

Evidence:
- Oral agents:
  - Meta-analysis of 43 randomized, controlled trials (RCTs), 9730 patients, example ~60-70% nail involvement, 12-16 weeks treatment. Rates of clinical cure after 4 months-2 years follow-up:
    - Terbinafine versus placebo, 8 RCTs: 48% terbinafine, 6% placebo, number needed to treat (NNT)=3.
    - “Azoles” (mostly itraconazole) versus placebo, 9 RCTs: 31% azole, 1.4% placebo, NNT=4.
    - Terbinafine versus “azoles” (mostly itraconazole), 15 RCTs: 58% terbinafine, 46% azole; NNT=9.
- Topical ciclopirox:
  - 3 RCTs, 928 patients, 48 weeks of treatment, ~40% nail involvement. “Cure” (mycological and clinical cure): 6-8% ciclopirox, 0-1% placebo (NNT=15-23).
- Topical efinaconazole:
  - 2 identical RCTs, 1655 patients. 48 weeks of treatment, assessed at 52 weeks, ~40% nail involvement:
    - “Complete cure” (mycological cure and 100% healthy nail): ~16%, ~4% placebo (NNT~9).
  - RCT, 135 patients. After 36 weeks of treatment and 4 weeks follow-up, ~40% nail involvement:
    - “Complete cure” (mycological cure and 100% healthy nail): ~22%, 9% placebo (NNT=8).

Other systematic reviews only reported mycological cure.
Context:
- While British guidelines suggest laboratory confirmation before treatment; only 50% of Canadian guideline authors recommend this approach. Only 50% of Canadian guideline authors recommend this approach.12
  - Culture results take several weeks and have ~35% false negative rate.13
  - Fungal stains alone (without culture/histology) have low sensitivity.13
- Canadian guidelines suggest topical efinaconazole if <20% nail involvement, efinaconazole +/- oral terbinafine for 20-60% involvement (or for >3 nails), oral terbinafine for >60% involvement.12
- Risk of terbinafine-induced liver injury: ~1 in 50,000-120,000 prescriptions.14
- Medication Costs:15
  - Oral (12 weeks):
    - Terbinafine: ~$90
    - Itraconazole: ~$850
  - Topical (48 weeks): 2 bottles per treatment.
    - Ciclopirox: ~$150
    - Efinaconazole: ~$250
- Terbinafine treatment without confirmatory testing is likely most cost-effective approach.16
- Although not always statistically different, some RCTs found clinically relevant improvements with 4-6-month oral treatment regimens compared to 3 months.3,17

Authors:
Adrienne Lindblad BSP ACPR PharmD, Stacy Jardine BScPharm, Michael Kolber MD CCFP MSc

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References:
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