Empiric Treatment of Onychomycosis with Terbinafine

Tessa Hovenden DO, PGY-2

University of Kansas School of Medicine- Wichita
Family Medicine Residency at Ascension Via Christi

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Tessa Hovenden, DO

Tessa Hovenden was born and raised in the beautiful state of Alaska. She received a bachelor's degree in Biology from the University of Alaska Fairbanks, attended medical school at Rocky Vista University College of Osteopathic Medicine and is now in her second year of family medicine residency at Via Christi Family Medicine in Wichita, KS.
Learning Objectives

At the end of this presentation, the learner should be able to:

- Identify the most cost-effective approach to treating a patient with clinically suspected onychomycosis
- Determine when it is appropriate to use confirmatory testing for clinically suspected onychomycosis
- Discuss the side effect profile, safety, and cost of medications used to treat onychomycosis
The Study

The Study

- Goal: determine most cost-effective evaluation/treatment of clinically suspected onychomycosis
  - Previous recommendations - always perform confirmatory testing before terbinafine (terbinafine was significantly more expensive at that time)
  - Modern cost analysis done for oral terbinafine and topical efinaconazole 10%
Why This is Important

- Onychomycosis prevalence 7-14% in adults in North America

- Potential for clinical misdiagnosis
  - Lichen planus, nail trauma, psoriasis, diabetes, bacterial infection, contact dermatitis, pachyonychia congenita, idiopathic onycholysis

- Updated guidelines needed to establish when to use confirmatory testing, keeping side effects, cost of testing and treatments in mind
Study Design

Three treatment arms

1. Immediate treatment for all patients with clinically suspected onychomycosis

2. In-clinic KOH screening
   - If positive, treatment initiated
   - If negative, proceed to Periodic acid-Schiff (PAS) testing

3. PAS testing
How to Collect Nail Scrapings

- Cleanse the nail with alcohol
- Scrape the top layer of the nail off with scalpel and discard
- Continue to collect scrapings, adequate sample size is >top of a thumb tack
- Also acceptable specimens:
  - Clippings from any discolored/brittle parts of the nail
  - Scrapings from under the edges of the nail

“KOH and FUNGUS CULTURE COLLECTION PROCEDURE.” FUNGUS CULTURE COLLECTION PROCEDURE, tests.northernplainslab.com/NPLTestCatalog/Collect/KOH_and_Fungus_Culture_Collection.htm
KOH Screening

- Nail scrapings put onto glass slide
- KOH solution drops added to slide
- Slide is heated
- KOH breaks down cellular structures and fungal components are released and become visible on slide

Image obtained from Google Images, used with permission
PAS (Periodic Acid Schiff) Testing

- Nail scrapings fixed in formalin
- Cells stained in lab by PAS protocol
- Fungi stains red/purple
Fungal Culture of Nail Scrapings

- Use in rare instances
- Collect nail scrapings and submit to lab in dry container at room temperature
- Results take 4-6 weeks
- Approximately 1/3 of cultures are false negatives
## Calculated Costs (Remain Constant)

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Terbinafine, 250-mg, full treatment course</td>
<td>$10</td>
</tr>
<tr>
<td>AST</td>
<td>$21</td>
</tr>
<tr>
<td>ALT</td>
<td>$22</td>
</tr>
<tr>
<td>KOH stain preparation in office</td>
<td>$6</td>
</tr>
<tr>
<td>PAS test</td>
<td>$148</td>
</tr>
</tbody>
</table>

• Cost analysis was performed across presumed disease prevalence of 30%, 60%, and 90%

• Actual disease prevalence based on confirmed PAS evaluation of patients in this study was 75%
Variable Costs  
(Vary across disease prevalence)

<table>
<thead>
<tr>
<th></th>
<th>30% prevalence</th>
<th>60% prevalence</th>
<th>90% prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate treatment</td>
<td>$53</td>
<td>$53</td>
<td>$53</td>
</tr>
<tr>
<td>KOH screening</td>
<td>$123</td>
<td>$108</td>
<td>$92</td>
</tr>
<tr>
<td>Direct PAS testing</td>
<td>$172</td>
<td>$183</td>
<td>$193</td>
</tr>
</tbody>
</table>

When using terbinafine: Across all prevalence rates, *confirmatory testing resulted in higher cost* in comparison to empiric treatment alone.
Additional cost of testing per patient to avoid one inappropriate treatment

<table>
<thead>
<tr>
<th>Prevalence, %</th>
<th>KOH screening</th>
<th>Cost, $^a</th>
<th>Direct PAS testing</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Terbinafine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>192</td>
<td></td>
<td>238</td>
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<tr>
<td>90</td>
<td>764</td>
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<td>1949</td>
</tr>
</tbody>
</table>

Concern for Hepatotoxicity

- Incidence of 1:50,000 to 1:120,000 prescriptions of terbinafine
- Most cases will spontaneously resolve 3-6 months after discontinuing terbinafine

Discussion

Terbinafine:

- Less expensive to treat empirically (without obtaining confirmatory tests) across a wide range of prevalence (30%-90%)

- Inappropriate treatment concerns due to adverse effect of hepatotoxicity
  - actual incidence of this is exceedingly low (1:50,000 – 1:120,000)
Discussion

Cost of LFT monitoring to avoid one case of clinically significant liver injury is somewhere between $9.62 million and $233.89 million

- Liver function testing recommended before initiating treatment and every 4-6 weeks during treatment
Limits of the study

- Cost analysis was performed using prices in the US, and is not generalizable internationally.

- Study assumes that health care professionals performing KOH testing and collecting nail scrapings for PAS testing were doing so correctly.
Social Determinants of Health

- Physical symptoms – bothersome
- Psychological symptoms: can be associated with feelings of low self esteem, poor body image, anxiety, depression, low self-worth
- Patients may be less likely to participate in social/leisure activities
Social Determinants of Health

- Economic burden: doctors visits, sick days (1.8:258 participants)
- More impactful in special populations: i.e. elderly, diabetics
- These social consequences tend to be worse in fingernail infections vs. toenail infections
Conclusions

- When using terbinafine, empiric treatment without confirmatory testing is safe and most cost-effective.

- If concerns, confirmatory testing and LFT should be used.


“KOH and FUNGUS CULTURE COLLECTION PROCEDURE .” FUNGUS CULTURE COLLECTION PROCEDURE, tests.northernplainslab.com/NPLTestCatalog/Collect/KOH_and_Fungus_Culture_Collection.htm.


Questions?
Thank you.