ADVANCED STRATEGIES IN FUNGAL NAIL MANAGEMENT

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CONFLICT OF INTEREST

RESEARCH GRANTS - TO UNIVERSITY
- Dusa, Meiji, Valeant, Viamet
- Amgen, Abbvie, Boehringer Ingelheim, Celgene, Lilly, Merck, Novartis, Pfizer

CONSULTANT - HONORARIUM
- Anacor, Celgene, Lilly, Pfizer, Valeant

Objectives:
- Diagnosis of Onychomycosis
  - Bedside and laboratory diagnosis
- Differential diagnosis
- New Topical Antifungal Agents
  - Efinaconazole and tavaborole solutions

Onychomycosis Highlights
- More common in toenails than fingernails
  - Fingernails only seldom occur
- Caused by dermatophytes, non-dermatophyte molds, and Candida
  - Tinea unguium - dermatophytes only
- Four subtypes that are named by the method of fungal invasion
  - DLSO most common and indication for treatment with topical and oral drugs

MANAGEMENT BEGINS WITH BEDSIDE DIAGNOSIS
- LOOK FOR: Distal onycholysis with subungual debris in toenails
- IGNORE: Thick nail plate - not diagnostic!
- OBSERVE: Fingernails, presence of tinea pedis or dermatophytoma
- ASK ABOUT: Present or past history of tinea pedis in patient and family members and risk factors - pedicures, gymnasiums, military history

ONYCHOLYSIS GENERALLY PRESENT

DISTAL LATERAL SUBUNGUAL ONYCHOMYCOSIS
LOOK FOR EVIDENCE OF TINEA PEDIS

TIP...

NO TINEA PEDIS = NO ONYCHOMYCOsis

Mocassin Tinea Pedis

Onychomycosis presence was a predictive factor

Sakka N et al Int J Derm 2015;54:146-149

221 asymptomatic subjects with “normal feet”
14% were culture positive T. rubrum
TINEA PEDIS CAN BE HIDDEN!

TINEA PEDIS MAY NOT BE OBVIOUS!

Look for Collarettes of Scale in T. Rubrum
Tinea Pedis

Collarettes of Scale Seen in T. rubrum
Infection

IF YOU THINK THERE IS ONYCHOMYCOsis...

...LOOK HARDER

Look for Collarettes of Scale to Confirm in Tinea Pedis
Dermatophytoma - Indicative of Onychomycosis

Yellow to orange streaks or patches

Dermatophytoma - Streaks and patches are fungal abscesses

Abnormal fingernails - look at toenails

Abnormal fingernails with normal toenails unlikely onychomycosis

Diagnosis of Onychomycosis
- Presence or absence of fungal elements
  - KOH / calcofluor
  - PAS stain
- Fungal identification
  - Fungal culture
  - PCR analysis

PAS stain for hyphae

PAS stain positive
**T. rubrum**

**MOST COMMON CAUSE OF ONYCHOMYCOSIS**

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**What About Diagnosis? Is There a Controversy?**

- Empiric treatment with terbinafine for patients with suspected onychomycosis is more cost effective than confirmatory testing with minimal effect on safety.
- Confirmatory testing before efinaconazole will reduce costs across a range of disease prevalence.

Mikailov A et al JAMA Derm 2015 online Dec 23

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**HALF OF ABNORMAL NAILS HAVE FUNGUS**

**THE OTHER HALF DO NOT!**

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**DIFFERENTIAL DIAGNOSIS**

- Lichen Planus
- Psoriasis
- Tumoronychomatricoma
- Trachonychia
- Onychogryphosis

**YELLOW NAIL SYNDROME**
TOPICAL ONYCHOMYCOSIS TREATMENT

- **SOLUTIONS:**
  - Efinaconazole 10%
  - Tavaborole 5%
- Non-lacquer alcohol based therapies can be delivered on, under and around the nail bed

**EFINACONAZOLE**

- **Triazole antifungal**
  - New molecule
- **Broad spectrum antifungal with activity against yeasts, molds and dermatophytes**

{[(R,3R)-2-(2,4-difluorophenyl)-3-(4-methylenepiperidin-1-yl)-1-(1H-1,2,4-triazol-1-yl)butan-2-ol]}

**Mycologic Cure Rates (Pooled Data)**

Source: package insert terbinafine and itraconazole

**Complete Cure Delayed Because of Slow Nail Growth**

Tavaborole Study Design

- Similar to efinaconazole study design—applied once daily for 48 weeks in mild to moderate disease
- Differences in studies:
  - No upper age limit in tavaborole study
  - Nails were 20-60% involved in tavaborole vs. 20-50% in efinaconazole

BORON IS FOUND IN FOODS: FRUITS, VEGETABLES AND NUTS
Some Failures Are Incorrectly Reported

TREATMENT FAILURE?

Elewski BE et al. Efficacy and safety of tavaborole topical solution. JAAD 73:02-09.2015

“FAILURES” SOME NAILS MAY NEVER BE NORMAL BUT FUNGUS NOT PRESENT AND OTHERS TAKE TIME TO GROW

“FAILURES” SOME NAILS BENEFIT FROM TOPICAL STEROID SOLUTION TO HELP NAIL ATTACH

Elewski et al. JAAD Epub 2012.

Other Considerations: Common Comorbidities that Prevent Normal Nails

- Psoriasis
  - High prevalence (about 30%) of onychomycosis with psoriatic toe nails
- Nail tumors and structural abnormalities
  - Onychomatricoma
  - Pincer nails
  - Yellow nail syndrome
  - Prior nail trauma
  - Onychogryphosis

KEY POINTS

- Bedside diagnosis
  - Presence of tinea pedis
dermatophytoma
- Half of abnormal nails caused by fungi
- Topical tavaborole and efinaconazole solutions effective treatments
MANAGEMENT OF ONYCHOMYCOSIS
Beyond Topical Monotherapy

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Disclosures

Allergan*+
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Viamet*+

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Develop a Rational Strategy Designed to Achieve Optimize Management of Onychomycosis

• Confirm diagnosis
  • Clinical examination
    • Putting together the pieces of the puzzle
  • Diagnosis – proper specimen collection!
    • Potassium hydroxide preparation (KOH)
    • Fungal Culture
    • Nail plate “biopsy” + Periodic Acid-Schiff (PAS) stain

• Physical modalities
  • Adjunctive and palliative measures
    • Debridement – physical, chemical
    • Avulsion
    • Removal of dermatophytoma

Develop a Rational Strategy Designed to Achieve Optimize Management of Toenail Onychomycosis

• Confirm diagnosis
  • Clinical examination
    • Putting together the pieces of the puzzle
  • Diagnosis – proper specimen collection!
    • Potassium hydroxide preparation (KOH)
    • Fungal Culture
    • Nail plate “biopsy” + Periodic Acid-Schiff (PAS) stain

• Physical modalities
  • Adjunctive and palliative measures
    • Debridement – physical, chemical
    • Avulsion
    • Removal of dermatophytoma

When to Use Oral Therapy for ONYCHOMYCOSIS

• Good General Rule: When the patient has onychomycosis!
• Rational choice for moderate to severe involvement
  • Nail plate thickness >4mm
  • >50% nail plate area involved (distal to proximal)
  • May be used for milder cases based on discussion with patient
  • May be used after discussion and review of potential adverse effects
  • May be used after exclusion of drug-drug interactions
  • Duration of therapy may need to be extended
  • Repeated courses or intermittent oral therapy may be warranted
• Frequent integration of COMBINATION THERAPY
  • Debridement / Removal of dermatophytoma
  • Oral + topical antifungal therapy
  • Oral + topical nail barrier therapy
Oral Therapy Options for ONYCHOMYCOSIS

- **GRISOFULVIN** – not recommended for treatment especially in adults

- **KETOCONAZOLE** – not recommended / risk >>> benefit

- **TERBINAFINE**
  - Highly active against dermatophytes
  - Continuous therapy once daily: toenails x 12 weeks; fingernails x 6 weeks
  - Laboratory monitoring based on patient-related factors and history
  - Low risk of symptomatic hepatotoxicity
  - Short list of potentially significant drug-drug interactions (CYP2D6)

- **ITRACONAZOLE**
  - Very good broad-spectrum antifungal activity
  - Continuous or pulse therapy regimens
  - Laboratory monitoring based on patient-related factors and history
  - Low risk of symptomatic hepatotoxicity / cardiotoxicity (CHF)
  - Long list of potentially significant drug-drug interactions (CYP3A4)

- **FLUCONAZOLE**
  - Very good broad-spectrum antifungal activity
  - Studies confirming efficacy and safety with intermittent (once weekly) dosing
  - Highly favorable safety profile
  - Negligible risk of drug interactions with once weekly dosing

ORAL THERAPY MAY BE USED IN COMBINATION WITH TOPICAL THERAPY AND/OR PHYSICAL MODALITIES

Methods to Expedite Therapeutic Outcomes with Oral Therapy for Onychomycosis

- **Pre-Debridement**
- **Immediate Post-Debridement**
- **Topical Barrier Repair**
- **SEM Cross Section**

Develop a Rational Strategy Designed to Achieve Optimize Management of Onychomycosis

- **Laboratory monitoring**
  - Oral Agents
  - Terbinafine
  - Itraconazole
  - Fluconazole
- **Think “Outside the Box”**
  - Prolong the duration of therapy
  - Intermittent therapy
  - Sustain efficacy
  - Prevent relapse or recurrence
  - Patient wants to use nail polish

References