Lasers and Lights for Onychomycosis

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Background

- Onychomycosis occurs when there is an overgrowth of fungus in the nail bed
- Not just a disorder of the elderly - incidence in children under 18 was found to be 0.44%
- In older and diabetic populations, however, onychomycosis can be more troubling - serving as a nidus for infection resulting in more serious complications.
- Notoriously difficult to treat
  - Topical agents are ineffective in penetrating nail plate and reaching nail bed
  - Oral antifungals have potential to cause adverse systemic side effects, which is more important given population where onychomycosis is most prevalent.

Currently, lasers are only FDA approved for the temporary increase in clear nail growth in patients with onychomycosis. NOT supposed to be advertised as a cure. Some currently FDA-approved systems for this indication:

- Mechanism of Action - Unclear
  - Direct inactivation of fungus by heat
  - Creation of ROS
  - Selective photothermolysis - exact chromophore not known

<table>
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<th>FDA approved for clear nail growth</th>
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<td>1320 nm Nd: YAG</td>
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<td>1064 nm Nd: YAG long-pulsed</td>
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CO2 Laser

- Oldest of the laser therapies studied for onychomycosis
- CO2 laser is ablative in nature, usually causing tissue destruction
- This can either destroy the fungus directly, or allow for better penetration of topical antifungals

- 2 studies found efficacy:
  - Apfelberg et al. (1984): 6/9 patients had clearance of organism with just one treatment. Study parameters not clearly defined
  - Borovoy et al. (1992): Nail plate fenestration with CO2 laser allows for better penetration of topical antifungals. One laser session + 12-18 mo. of topicals. Complete clearance in 75% at 3yr follow-up

- Newer, less invasive laser options are currently available
UV light is germicidal to bacteria and fungi.
Also damaging to human tissue (known mutagen), limiting its role. UV blockers may be of benefit.

Potential role of UV light (UVC) alone for onychomycosis
- One ex vivo study. Found 100% inactivation of T. rubrum in nail fragments without resistance.

Effect of UVA light in PDT
- UVA light + synthetic photosensitizers were fungicidal to T. rubrum on stratum corneum independent of fungal growth stage.

Most studied light modality for onychomycosis
- Photosensitizing agent can be 5-ALA or other synthetic agents.
  - Experimental synthetic agents include light-activated porphyrins Sytens B and Duteroporphyrin monomethylester (DPmme).

Idea: fungi and yeast convert 5-ALA to protoporphyrin IX.
Protoporphyrin IX possesses a peak wavelength absorption between 630-700nm, making it easily targeted by red light.

Clinical trial
- Only clinical trial was following nail avulsion:
  - 30 patients
  - Removal of the nail after urea for 10 nights
  - 20% 5-ALA (3hr) + red light x 3 sessions
  - 43.3% mycological cure at 1yr follow-up.

870/930 nm
- Found to be fungicidal and bactericidal in vitro, spawning clinical evaluation.
- 4 sessions: 870/930 nm laser + 930 nm laser alone. Clear nail growth seen in 4/7 patients at 2 month follow-up. Nail cultures negative for all at 60 days.
- RCT: same settings as above. 44 patients underwent treatment in the experimental group and 15 patients were in the control group (exposed to sham light). 39% of nails had at least 3mm clear nail growth 4 months after last treatment. Improvement in 77% of cases noted by independent panel. No adverse events reported. 39% maintained negative cultures at 9 months follow-up.
1064 nm and 1444 nm Nd:YAG

- Longer wavelength — more deeply penetrate tissue and efficiently target fungal overgrowth in the nail bed
- Unfortunately, in vitro effects of Nd: YAG laser systems on T. rubrum growth have produced conflicting results
  - 2 studies, same settings (Q-switched 1064 nm, 4 and 8 J/cm², 2 mm spot size)
  - One study showed settings were effective in inhibiting T. rubrum colony growth.¹
  - Second study found no inhibitory, fungicidal or fungistatic effects²

¹ Vural E et al. (2008) The effects of laser irradiation on Trichophyton rubrum growth

Clinically, more promising results with 1064 nm

- Hochman 2011: 223 J/cm², 0.65 ms pulse, 2 mm spot size, 2 passes; 2-3 sessions/3 weeks; 87.5% had negative cultures immediately after final treatment
- Kimura 2012: 14 J/cm², 0.30 ms pulse, 5 mm spot size, 2 passes; 2-3 sessions/4 or 8 weeks; 51% had negative cultures at 6 months

- Similar peak powers (13.7 J/ms & 11.6 J/ms)

Future directions:
Femtosecond IR Titanium Sapphire Laser (800 nm)

- Femtosecond lasers are lasers that maintain a pulse duration of 10⁻¹⁵ seconds
- They break down transparent or semi-transparent biological tissues due to nonlinear absorption of laser energy with minimal thermal and mechanical effects
- Manevitch and colleagues found that a sufficient therapeutic window exists where in vitro fungal growth can be completely inhibited without affecting the structure of the nail plate
- Elimination of the fungus confirmed with SEM
- In vivo, clinical studies needed

Choi MJ et al. (2012) Antifungal effect of a 1,064-nm Nd:YAG laser on Wistar rat nail plate with Trichophyton rubrum or Candida albicans
Manevitch Z et al. (2010) Direct antifungal effect of femtosecond laser on Trichophyton rubrum onychomycosis
Indications & Contraindications

- Clinically and mycologically confirmed onychomycosis by:
  - Direct microscopy
  - Fungal culture
  - Culture + PAS = most sensitive (94%) but may take long time

- Cannot tolerate, do not want other procedures
- Able to maintain adequate hygiene between sessions

- Unable to tolerate light therapy
- Seizure disorder
- LE
- Gout therapy
- Certain medications
- Caution with peripheral neuropathy

Pre and Post-Op Care

- Rule out other causes of dystrophic nails
- Obtain cultures for identification of species, if possible
- Discuss expectations with patients - Clear nail growth is not guaranteed and may take many sessions. Re-infection is possible
- May need urea pretreatment

- No wound care necessary
- Patients encouraged to keep feet dry and rotate shoes and socks (+/- powder)
- Topical antifungal cream between sessions may help to prevent recurrence

Complications and Safety Measures

- Reported incidence is low
- Pain, heat or tingling during procedure
- Temporary darkening under the nail possible
- Temperature probe for patients with peripheral neuropathy

Our Experience

- 980 nm diode laser
- 7 patients
- Each session, treat until patient reports feeling warmth. Treatment stopped if too hot for comfort.
- Sessions varying between 2 and 6 sessions +/– topical antifungal cream in between sessions
5 month f/u

* 3rd and 6th sessions

6 month f/u

* 2nd and 5th sessions

3 month f/u

* 2nd and 3rd sessions

Summary

- Role of lasers and PDT are being explored in the treatment of onychomycosis
- Mechanism of action is not fully understood
- Further studies are warranted to clarify lasers and lights for the treatment of onychomycosis
Thank You