The Efficacy and Safety of 1064 nm Nd:YAG Laser in the Treatment of Onychomycosis – Thai Experiences

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Background

- Onychomycosis is a common nail disease, especially in elderly people.
- Multiple treatment modalities with limitations.

Mechanical debridement

Topical antifungal agents

Chemical debridement

Systemic antifungal agents
Background

However, their limitations include:

- High failure rate
- Time-consuming
- Pricing
- High risk of drug interaction

Previous study about treatment of dermatophyte onychomycosis with long-pulsed 1064 nm Nd:YAG laser (Dualis SP; Fotona, Slovenia) demonstrated excellent outcome (cure rate 95.38% at 3-month FU, 100% at 6-month and 12-month FU) without severe side effects.

The laser penetrates through the nail plate and produces heat deep within the dermis and nail tissue (desired average tissue temperature 43-51 °C).

One of the main advantages is fungicidal effect (destruction of pathogenic organisms and stimulation of the repairative process).
In western countries, the proportion of dermatophyte onychomycosis is nearly 90 percent of all fungal nail infections.

But there is higher prevalence of nondermatophyte onychomycosis in Thailand (~ 50 % of all fungal nail infections).

In theory, laser treatment in dematiaceous nondermatophyte onychomycosis seems to be good response due to containing of melanin pigment.

Objective

- To evaluate mycological results and side effects of onychomycosis treatment with long-pulsed 1064 nm Nd:YAG laser

- Dermatophytes
- Nondermatophytes
- Yeasts
- Mixed infection

??
Inclusion criteria

- Aged >18 years was diagnosed onychomycosis by mycological laboratories
- No Hx of isotretinoin and/or vasodilators 6 months before recruitment
- No Hx of topical and/or systemic antifungal agents 6 months before recruitment
- Informed consent form, approved by the Ethical Committee was signed by all subjects
Exclusion criteria

- Pregnancy
- Breastfeeding
- Permanent or semi-permanent discoloration of nail plate
- Other skin lesion was presented at the treatment site such as psoriasis, subungual hematoma
Methods

- SIRB approved study
- **92 onychomycotic nails** are needed
- Until now, **40 onychomycotic nails** from 21 patients were recruited to the study
Methods

- All nails were only treated with long-pulsed 1064 nm Nd:YAG laser (Dualis SP; Fotona, Slovenia) four sessions with a week interval in every cycle.
- Mycological results (Potassium Hydroxide examination and fungal culture) were taken every treatment and follow-up visits.
Laser parameter of long-pulsed 1064 nm Nd:YAG laser (Dualis SP; Fotona, Slovenia) was

- 35-45 J/cm² of fluence
- 30-35 msec of pulse duration
- 4 mm of spot size
- 1 Hz of frequency
At each treatment visit, the entire nail plate was treated in spiral pattern for 3 passes with 2 minutes pause in between.
Objective evaluation

- KOH (every treatment and follow-up visits)
- Fungal culture (every treatment and follow-up visits)

Subjective evaluation

- Photograph (Before treatment, F/U 1 mo, F/U 3 mo, F/U 6 mo)
- Nail severity index (Before Treatment, F/U 1 mo, F/U 3 mo, F/U 6 mo)
- Pain score (0-100) (1st treatment)
- Adverse effect evaluation (every treatment visits)
## Results

### Age (years)

<table>
<thead>
<tr>
<th>N</th>
<th>40</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean</strong></td>
<td>62.68</td>
</tr>
<tr>
<td><strong>Median</strong></td>
<td>67.00</td>
</tr>
<tr>
<td><strong>Standard deviation</strong></td>
<td>10.97</td>
</tr>
<tr>
<td><strong>Minimum</strong></td>
<td>39</td>
</tr>
<tr>
<td><strong>Maximum</strong></td>
<td>82</td>
</tr>
</tbody>
</table>
## Type of onychomycosis

<table>
<thead>
<tr>
<th>Type of onychomycosis</th>
<th>Number of nails</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distal and lateral subungual</td>
<td>36 (90%)</td>
</tr>
<tr>
<td>Superficial white</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Proximal subungual</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Total dystrophic</td>
<td>4 (10%)</td>
</tr>
</tbody>
</table>
## Fungal isolation

<table>
<thead>
<tr>
<th>Type of fungal isolates</th>
<th>Number of nails</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Trichophyton rubrum</em></td>
<td>13 (32.5%)</td>
</tr>
<tr>
<td><em>Trichophyton mentagrophytes</em></td>
<td>11 (27.5%)</td>
</tr>
<tr>
<td><em>Scytalidium dimidiatum</em></td>
<td>13 (32.5%)</td>
</tr>
<tr>
<td><em>Fusarium solani</em></td>
<td>2 (5%)</td>
</tr>
<tr>
<td>Co-infection (<em>T. rubrum</em>+<em>S. dimidiatum</em>)</td>
<td>1 (2.5%)</td>
</tr>
</tbody>
</table>
Results: 1st cycle of treatment

- 40 nails (21 patients)
  - Continue 1st cycle of treatment
    - 40 nails
  - Loss follow up
    - 4 nails
  - during 1st cycle
    - 1 nail
  - +ve pathogenic org. after 1st cycle
    - 22 nails
  - -ve pathogenic org. after 1st cycle
    - 13 nails

62.86% 37.14%
Results: 2nd cycle of treatment

Continue 2nd cycle of treatment
22 nails

15 nails

+ve pathogenic org. after 2nd cycle
14 nails

93.33%

-ve pathogenic org. after 2nd cycle
1 nails

6.67%

during 2nd cycle
7 nails
Our study vs. Dr. Kozarev’s study

- Cure rate < 40% vs 95.8%
- Same machine
- Same treatment protocol
- Same treatment parameter
- Same technique
## Our study vs. Dr. Kozarev’s study

<table>
<thead>
<tr>
<th></th>
<th>Our study</th>
<th>Dr. Kozarev’s study</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>Mean = 62.68</td>
<td>18-45</td>
</tr>
<tr>
<td><strong>Fungal Isolation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- T. Rubrum</td>
<td>32.5%</td>
<td>51.4%</td>
</tr>
<tr>
<td>- T. mentagrophytes</td>
<td>27.5%</td>
<td>30.5%</td>
</tr>
<tr>
<td>- S. dimidiatum</td>
<td>32.5%</td>
<td>-</td>
</tr>
<tr>
<td>- Others</td>
<td>7.5%</td>
<td>18.1%</td>
</tr>
</tbody>
</table>
Table II. Poor prognostic factors

1. Areas of nail involvement > 50%
2. Significant lateral disease
3. Subungual hyperkeratosis > 2 mm
4. White/yellow or orange/brown streaks in the nail (includes dermatophytoma\textsuperscript{14})
5. Total dystrophic onychomycosis (with matrix involvement)
6. Nonresponsive organisms (eg, Scytalidium mold)
7. Patients with immunosuppression
8. Diminished peripheral circulation

### Poor Prognostic Factors

<table>
<thead>
<tr>
<th></th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(22 nails)</td>
<td>(13 nails)</td>
</tr>
<tr>
<td>Mean age (year)</td>
<td>62.59 ± 11.69</td>
<td>62.69 ± 11.54</td>
</tr>
<tr>
<td>Area of involvement &gt;50%</td>
<td>4.55%</td>
<td>23.08%</td>
</tr>
<tr>
<td>Significant lateral disease</td>
<td>13.64</td>
<td>7.70%</td>
</tr>
<tr>
<td>Subungual hyperkeratosis (mm)</td>
<td>2.16 ± 0.94</td>
<td>1.27 ± 0.53</td>
</tr>
<tr>
<td>Yellow streaks in nail</td>
<td>13.64%</td>
<td>7.70%</td>
</tr>
<tr>
<td>Total dystrophic nail</td>
<td>13.64%</td>
<td>7.70%</td>
</tr>
<tr>
<td>Nonresponsive organism</td>
<td>45.45%</td>
<td>30.77%</td>
</tr>
<tr>
<td>Diminished peripheral circulation</td>
<td>22.73%</td>
<td>0%</td>
</tr>
</tbody>
</table>
Results: case 1 (Lt. big toe)

Scytalidium dimidiatum

Pretreatment

4 months

positive for pathogenic organism

1-mo after the 2nd cycle
Results: case 13 (Rt. big toe)

Trichophyton rubrum

Pretreatment

4 months

negative for pathogenic organism

1-mo after the 2nd cycle
## Pain score

<table>
<thead>
<tr>
<th>Pain score</th>
<th>Number of nails</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intolerable pain (76-100)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Severe pain (51-75)</td>
<td>7 (17.5%)</td>
</tr>
<tr>
<td>Moderate pain (26-50)</td>
<td>13 (32.5%)</td>
</tr>
<tr>
<td>Mild pain (1-25)</td>
<td>16 (40%)</td>
</tr>
<tr>
<td>No pain (0)</td>
<td>4 (10%)</td>
</tr>
</tbody>
</table>
## Adverse effects evaluation

<table>
<thead>
<tr>
<th>Adverse effects</th>
<th>Number of nails</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythema</td>
<td>Mild, 1 (2.5%)</td>
</tr>
<tr>
<td>Swelling</td>
<td>Mild, 3 (7.5%)</td>
</tr>
<tr>
<td>Blister</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Post inflammatory hyperpigmentation</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Post inflammatory hypopigmentation</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>
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DISCUSSION
Is the laser treatment worth it? 

< 40% cure rate at 1 month follow-up after complete 1\textsuperscript{st} cycle of laser treatment
An open randomized comparative study of oral itraconazole pulse and terbinafine pulse in the treatment of onychomycosis.

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**Table 3: Evaluation schedule of patients**

<table>
<thead>
<tr>
<th>Weeks of follow up</th>
<th>No. of patients showing clinical cure</th>
<th>No. of patients showing mycological cure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group A (itraconazole)</td>
<td>Group B (terbinafine)</td>
</tr>
<tr>
<td>Week 4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Week 8</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Week 12</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Week 16</strong></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Week 24</td>
<td>24</td>
<td>10</td>
</tr>
<tr>
<td>Week 36</td>
<td>31</td>
<td>34</td>
</tr>
<tr>
<td>Week 48</td>
<td>41</td>
<td>39</td>
</tr>
</tbody>
</table>

\[ n = 60 \quad n = 60 \]
What can we do to improve the efficacy of laser treatment?
Efficacy and safety of 1% clotrimazole cream occlusion with the mechanical reduction as an adjuvant therapy for the treatment of onychomycosis

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Fig. 3 Pretreatment and posttreatment nail thickness: this table shows difference of nail thickness grading between the control and study group at 3 months (p = 0.001)
Subungual hyperkeratosis

**Conclusion**: The mechanical nail reduction by nail filing plus 1% clotrimazole cream occlusion as adjuvant therapy was demonstrated to provide safety and efficacy for onychomycosis therapy. It significantly reduces time to cure and nail thickness; and minimizes health care cost more than only conventional oral antifungal drug.
Conclusions

- Long-pulsed 1064 nm Nd:YAG laser therapy is **safe and effective** in treatment of onychomycosis.
- In patients with **poor prognostic factors**, laser treatment should be used in combination with other treatment.
- Other mechanical modality may also be useful.
- However, **larger sample size and longer follow-up term** are needed.
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THANK YOU