

# A Novel Method for the Treatment of Fungal Nail Disease with 1064 nm Nd:YAG

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## ABSTRACT

A novel laser method for the treatment of fungal nail disease with 1064 nm Nd:YAG was clinically evaluated on a Ukrainian patient population. 108 patients exhibiting 312 infected nails were treated with 1064 nm Nd:YAG laser (SP Dynamis, Fotona, Slovenia) at a single clinical site over a period of two years (2010-2012). All patient were diagnosed with one of four types onychomycosis, caused by various fungi. Diagnoses were performed by laboratory testing of mycotic cultures. All patients received four sessions of laser treatment and were again checked by laboratory tests at 3 and 6 months after the treatment. Any patients found to have positive cultures at 3-month follow-ups were retreated.

In addition to laboratory checks at 3 and 6 months, patients were also clinically inspected at 3, 6 and 12 months, when photographs of all treated nails were taken and clearance of the nail plates and thus clinical improvement was evaluated by two physicians. Discomfort during treatment was evaluated by patients and potential side effects were monitored. At the 12-month follow-up, 89 patients (82.4%) were cured; 80 of which (74.1%) had negative fungal cultures and 9 (8.3%) showed clinical improvement, while 19 patients (17.6%) were non-responsive to the therapy.

Only mild discomfort during treatment was recorded and there were no other adverse effects. The study results showed that 1064 nm Nd:YAG laser treatment of onychomycosis is an effective and safe therapy that may be used in a broad spectrum of patients, including some groups of patients not suitable for systemic antifungal therapies.

**Key words:** nails fungal infection, onychomycosis, Nd:YAG laser, laser treatment

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## I. INTRODUCTION

Onychomycosis is a common infection of the nail, affecting approximately 17% of the Ukrainian population aged 30-40 years, with a morbidity rate between 32-40% at 70 years of age [1]. It affects immunocompromised individuals, smokers and patients with peripheral vascular disease, and those with a history of trauma to the nail or a family history of onychomycosis [2]. It is caused predominantly by anthropophilic dermatophytes (*Trichophyton Rubrum*, *Trichophyton Mentagrophytes*, etc.) which account for more than 90% of all cases, and to a lesser extent by yeasts (e.g. *Candida*) and non-dermatophyte molds (*Aspergillus niger*).

Contributing factors in the development of onychomycosis include:

- somatic diseases: diabetes, endocrine pathology, cancer diseases, vascular diseases, obesity;
- physiological states: menopause, hyperhidrosis;
- reduced local immunity;
- dystrophic disorders of the nail bed (slowing of nail growth);
- physical factors;
- mechanical damage to the nail (injury);
- chemical factors (constant contact with water, degreasing detergent, etc.).



Fig. 1: Onychomycosis manifestation.

Nail fungus infection is always secondary, that is, pre-fungus first affects the skin of the hands or feet, and only then infects the nail. A healthy nail plate is impervious to the fungus. Infection of the nail bed usually spreads from the edges to the ends of the nail. Gradually, the fungus spreads under the nail plate until it reaches the nail matrix.

Classification of onychomycosis (Zaias N., 1972):

1. Distal/lateral subungual onychomycosis – the nail bed is affected starting from the edges of the nail, the nail plate becomes whitish, changing its shape, and the nail becomes uneven, crumbling;

2. Superficial onychomycosis (endonyx) - whitish spots appear on the surface of the nail that grow, and after a while, cover the entire nail plate;

3. Proximal onychomycosis – fingernails are at first affected from the nail fold, from there the lesion extends to the nail matrix;

4. Total dystrophic onychomycosis – the nail plate is rough, thickened, whitish-yellow in color with subungual hyperkeratosis.

Some nail diseases, such as psoriasis, atopic dermatitis, nail trauma, contact irritants, and lichen planus can mimic onychomycosis, making the diagnosis additionally difficult, so laboratory monitoring before treatment is necessary for proper diagnosis.



Fig. 2: Psoriasis of the nail.



Fig. 3: Example of Onycholysis.

Various topical and oral therapies have been used in the past to treat onychomycosis. To date, the most common and generally accepted standard treatment for fungal nail infections is oral systemic antifungal therapy, sometimes combined with topical antifungals. Since the nail plate is an extremely dense structure through which topical antifungals hardly penetrate into the tissue, most topical agents are not very successful [7]. On the other hand, antifungal agents administered systemically represent a particular problem, since the therapy is long (3 to 12 months), expensive and

accompanied by a series of significant side effects. The most common systemic oral antifungals are: Lamisil, Gris-PEG and Sopranox, with the active ingredients: terbinafine, griseofluvin and itraconazole. Unfortunately, the effectiveness of the systemic treatment is low and varies according to different authors from 40 to 68-80% [8-11]. In particular, the efficiency of treatment decreases with age due to a slowing of metabolism and microcirculation in the nail bed, and with considerable hyperkeratosis. Especially problematic are some of the adverse effects of systemic antifungals. The FDA has issued warnings about the side effects of the systemic antifungal drugs Lamisil and Sopranox [12]. Side effects commonly include nausea and headaches and, although rarely, can include liver failure, heart problems, which can (and have) caused death. Elderly patients and immunocompromised patients should have their liver enzymes monitored during treatment. Also systemic antifungal drugs interact with other medications patients might be using and such interactions could also cause very severe adverse effects.

So, although systemic antifungal therapy is today commonly used, it cannot be assigned to all patient populations due to the above-mentioned risks. Elderly, children, immunocompromised patients, women during pregnancy and lactation, congestive heart failure patients and many others are definitely not suited for systemic antifungal therapy.

The rapid development of science in recent years has in large part shaped the needs of patients. To date, the customer of a dermatology clinic not only wants to be cured or have an aesthetic problem resolved, he/she also seeks to obtain this result using the most modern techniques, in the most comfortable, rapid, effective and safe way possible.

Recently, new data has appeared about treating nail fungal infections using novel techniques, including photodynamic therapy [13,14] and lasers [15-17]. Special interest was allocated to laser therapies since initial studies presented promising results, with quicker therapy and a very low rate of potential side effects. Although there are already several laser systems for the treatment of onychomycosis approved by the FDA, there are still no reliable, larger clinical studies with long-term observations in which significant clinical improvement was achieved. The most encouraging results were obtained by Dr. Kozarev using a Nd:YAG laser with a wavelength of 1064 nm [14]. In our research, we set out to test the effectiveness of laser therapy for onychomycosis and to find out the real possibilities and limitations, as well as the long-term prospects for recovery.

We were the first clinic in the Ukraine which tested a Nd:YAG 1064 nm laser for treatment of onychomycosis. Our first trials started at the end of 2010, and within two years we developed a unique method of treatment and conducted a relatively long follow up period (to 18 months). To date, after more than two years of performing this therapy, we have extensive experience and an understanding of the long-term effects, and through this paper we will share these findings with colleagues.

## II. MATERIALS AND METHODS

Over a period of two years (December 2010 - December 2012) we treated 108 patients with an established diagnosis of onychomycosis. Only patients with a diagnosis confirmed by laboratory, regardless of the severity of the clinical picture, were included into this study. Patients had between one and eleven nails affected (in total there were 312 affected nails), with a large majority having fungal nail infection of their toenails (102 or 94.4%), while only 6 patients (5.6%) had infections on finger nails.

Patients using photosensitive drugs or being on other antifungal therapies were excluded from this study. The other major exclusion criterion was pregnancy.

All patients were informed about the risks and benefits of the proposed laser therapy as well as about other treatment possibilities, and all also signed a written informed consent form. The Declaration of Helsinki, as well as the principles of good clinical practice, were respected in the execution of this study.

The efficacy of the treatment was observed visually (by clinical inspection of the nail and with comparison of photos) and with laboratory findings (direct microscopy) at 3, 6 and 12 months after treatment. An additional follow-up via telephone interview was performed at 18 months, at which patients were asked to report about their nail status (clear and healthy looking or not).

All patients were prescribed a course of laser therapy with a 1064 nm Nd:YAG laser (SP Dynamis, Fotona, Slovenia), which consisted of four sessions of laser therapy with an interval of 7 days between the sessions. The laser beam was applied to the entire infected nail as well as to the skin surrounding the nail.

We used a fluence of 35-40 J/cm<sup>2</sup> with a pulse duration of 35 msec at a 4 mm spot. Two passes with a two-minute interval were applied to every infected nail. There was no post-op care prescribed, except that

all patients were given advice on the prevention of reinfection at home.

The patients with positive mycotic findings on the first follow-up were re-treated using the same protocol.

In cases where patients had hyperkeratotic nails (poor prognostic factors according to RK Sher, 2007), they were advised to file the nail, making it thinner for better penetration of the laser beam. Such pre-treatment was required only in 6 of 108 patients (5.6%).

The mechanism of action in laser therapy is a photo-thermal effect and heating of the irradiated fungal cells. When the temperature rises above 43-51 degrees, denaturation of the proteins of fungal cells starts as well as the increased production of heat shock proteins (HSP). Exposed to repetitive increases of temperature, the fungi cease reproduction and growth, and with the continuation of the increased temperature begin apoptosis [15].

During the laser therapy, the surface nail temperature reached around 50 degrees C, which could be painful; thus air cooling was used (Cryo 6, Zimmer, Germany) to minimize patient discomfort. Patients were asked to evaluate the level of pain on a five point scale (0 = no pain, 1 = mild pain, 2 = medium pain, 3 = strong pain and 4 = very strong pain). Also, patients were asked to report about any other adverse effect they noticed during the treatment or in the post-treatment period.

## III. RESULTS

The patients' average age was 39.4 years (range: 18-74), 70 of who were female and 38 male), with Fitzpatrick skin types of I-III. Most had the distal subungual type of onychomycosis (88.9%). Among other types, total dystrophic was found in 7 cases (6.5%), proximal subungual in 3 cases (2.8%) and endonyx in 2 cases (1.8%). The distribution of onychomycosis types is presented in Table 1.

**Table 1: Onychomycosis types**

Onychomycosis type	Number of patients
<i>Distal subungual</i>	96 (88,9%)
<b><i>Endonyx</i></b>	<b>2 (1,85%)</b>
<i>Proximal subungual</i>	3 (2,78%)
<b><i>Total dystrophic</i></b>	<b>7 (6,48%)</b>
<b>Total</b>	<b>108 (100%)</b>

Regarding the fungi type (see Table 2), the most present type was *Trichophyton rubrum*, detected in 78

patients (72.2%), the next was *Trichophyton mentagrophytes*, found in 17 patients (15.7%), followed by *Candida* species (10 patients or 9.3%) and finally *Aspergillus niger* (3 patients or 2.78%).

**Table 2: Types of fungi found in the studied patient population.**

Fungi type (microbiologic)	Number of patients
<i>T.rubrum</i>	78 (72,2%)
<i>T.mentagrophytes</i>	17 (15,74%)
<i>Candida spp.</i>	10 (9,26%)
<i>Aspergillus niger</i>	3 (2,78%)
Total	108 (100%)

A total of 89 patients (82.4%) were found to be cured at last follow-up at 12 months after the treatment. 80 of these had negative mycological laboratory findings (checked at 3 and 6 months) and 9 were showing clinical improvement.

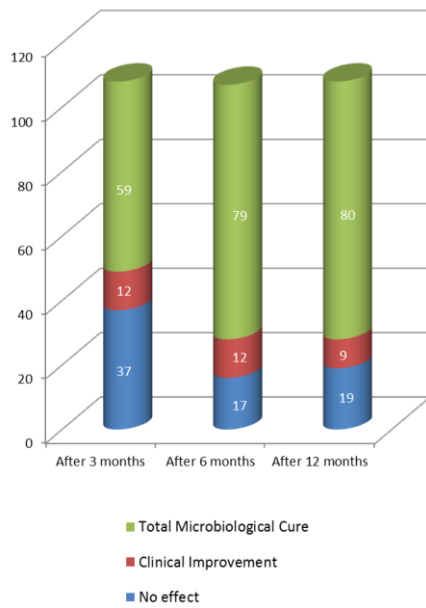


Fig. 4: Results of Nd:YAG laser therapy after 3, 6 and 12 months.

The laser therapy was not successful in 19 clinical cases (17.6%), of which 3 patients had concurrent onychomycosis and psoriatic nails. In 10 non-responding patients, onychomycosis was caused by moldy flora (*Asperogillus niger* and *Candida spp.*), and in two cases the patients had a recurrence of onychomycosis. In 9 cases we found clinical improvements of 30-50%, but mycological sterilization was never observed at laboratory check-ups, despite the second course of the laser treatment.

37 patients were found to be positive on laboratory

tests at 3-month follow-ups and were retreated and again checked after 3 months (at the otherwise 6-month follow-up). 20 of these were cured while 17 remained non-respondent.

Two patients became re-infected between the 6 and 12 month follow-ups, bringing the number of non-cured cases to 19 (or 17.6%).

We are continuing to observe our patients, and at 18 months conducted telephone interviews asking patients to describe the visual appearance of their nail(s) and to report about any other sign of disease recurrence. So far we have interviewed 13 cured patients, all of whom have reported to remain free of fungal infection at 18 months after the laser therapy.

All patients evaluated the pain during the therapy. While 38 patients (35.2%) didn't feel any pain, the majority of them (61 or 56.5%) reported mild pain and 9 (8.3%) reported medium pain.

There were no other adverse effects of this laser therapy noted.



Fig. 5: Patient A: before and after 6 months (*T. Rubrum*).



Fig. 6: Patient B: before and after 9 months (*T. Rubrum*).



Fig. 7: Patient B: before and after 9 months (Candida spp.).

#### IV. DISCUSSION

Several photographs (Fig. 5 to Fig. 10) are presented that confirm a positive trend – the growth of clear nail plates – in the cases of onychomycosis laser therapy using the Fotona Nd:YAG laser at 1064 nm. We believe that the fungistatic and fungicidal effects in this therapy are achieved due to the absorption of the 1064 nm laser wavelength in fungi tissues, producing a temperature increase which is the main factor of fungi destruction.

We found that both types of Trychophytons (Rubrum and Mentagrophytes) are effectively eradicated with the laser (88.4% for T. Rubrum and 94.1% for T. Mentagrophytes) and that these results correspond nicely with the results of some other authors [15]. On the other hand, we found that fungal infections caused by mold and yeast flora were poorly treatable with this laser therapy. Out of 10 cases of Candida we cured only 4 (40%), while we didn't succeed at curing any of the three cases of Aspergillus niger. In contrast to our experience, Dr. Kozarev [15] successfully cleared both of these types of fungal flora. Thus far we were not able to find the reason for such differing results. The truth is that the number of our patients having these infections was rather small and we hope that over time, collecting more cases, we should be able to achieve better results with this particular issue.



Fig. 8: Patient Z: before and after 12 months (T. Rubrum).

Comparing laser therapy with standard antifungal treatment, we found the following advantages: a significant reduction in treatment time (3 weeks versus 3-12 months of therapy), an absence of adverse effects (except for slight and short discomfort), quick and easy performance, and complete safety for patients and their body tissues during use.



Fig. 9: Patient O: before and after 12 months (T. Rubrum).

The results indicate that laser treatment should be the preferred method in cases of destructive dermatophyte flora with a slight lesion (up to 50% of a single nail) or when standard therapy techniques may not be used (for children, women during lactation, patients with severe hepatic impairment, the elderly) and also as an initial local treatment before the appointment of the standard course of treatment with systemic drugs.



Fig. 10: Patient P: before and after 6 months (T. Rubrum).

#### V. CONCLUSIONS

Laser treatment (1064 nm Nd:YAG) proved to be a highly effective tool enabling physicians to perform a modern and fast method of sterilization of the nail plate.

Potential shortcomings of this method could be (according to our limited data) lower effectiveness in the treatment of onychomycosis caused by moldy flora

(yeast, aspergillum resulted in no more than a 40% cure rate) and comorbidity (nail psoriasis). However, other researchers have reported good-to-excellent results in the treatment of moldy flora, and we are planning to do more researches to clarify this issue.

In general, given our findings, we could conclude that laser therapy for onychomycosis using 1064 nm Nd:YAG (SP Dynamis, Fotona) is highly efficacious new method (83% cure rate), applicable to the broadest patient population and having long-lasting results.

The treatment proved to be free of unwanted side effects, causing only mild heat discomfort for a short-time, easily tolerable by all patients treated.

We are continuing observations of our patients with the aim to establish data about the long-term efficacy of this method.

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