Laser Treatment of Nail Fungal Infection

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Figure 1. T. mentagrophytes. Before and after 6, 12 months

ABSTRACT

A clinical pilot study was conducted in which 42 nails from 14 patients who exhibited onychomicosis caused by Trichophyton sp., Aspergilus niger, Candida sp. and other molds were treated with a novel 1064 nm Nd:YAG laser therapy in a series of 4 sessions at 3 month intervals. In 13 (93%) of patients mycological clearance was observed at 3 month follow up, at 6 and 12 month follow up all patients were free of onychomicosis.

BACKGROUND AND OBJECTIVE

A combination of topical and oral antifungals is widely used to treat onychomycosis. Although recent progresses in oral antifungal agents have made it possible to treat onychomycosis effectively, these drugs can have considerable adverse liver and kidney effects and medication interactions in special populations, such as children, the elderly, and patients with underlying liver or systemic diseases. There is a great need for a simple, effective, nontoxic procedure that carries no risk of causing fungal resistance.

The primary aim of the study was to evaluate the efficacy and safety of novel laser therapy in the treatment of onychomycosis. We have investigated in vivo topical laser photobiology inactivation of the Trichophyton sp., Aspergilus niger, Candida sp. and molds with a long pulse Nd:YAG laser

(SP Dualis, Fotona). A long pulse NdYAG laser employs a near infrared wavelength of 1064 nm, which is well known to cause cellular photodamage in the absence of exogenous dyes or other photosensitive drugs and chemicals.

MATERIALS AND METHODS

Forty-two nails of 14 patients having clinically and mycologically proven onychomycosis, were submitted to transcutaneous laser irradiation with the aim of deactivation and eradication of fungal infection.

Study Criteria

Inclusion criteria:
Toenail fungus, finger nail fungal infection.
Ages: between 18-45 years old.

Clinical types of fungal nail infection:

- Total dystrophic form
- Distal subungual onychomycosis
- Proximal subungual onychomycosis
- Endonyx onychomycosis
- Signed Informed Consent

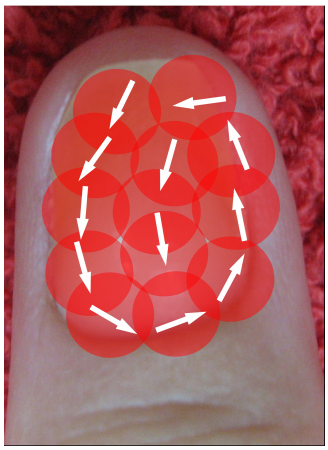

Figure 2. Laser scanning in the spiral pattern over affected nail.

Exclusion criteria:

- systemic antifungal therapy
- use of topical antifungal therapies such as solutio Castellani, which change nail pigmentation
- use of nail coloring dyes which change nail pigmentation
- use of photosensitivity inducing medications
- pregnancy
- children under 12 years of age if using any of above mentioning drugs
- existence of subungual hematoma or nevoid subungual formation
- existence of bacterial nail infection, which resulted in nail pigmentation
- existence of concomitant nail disorders such as psoriasis of nail plate, lichen planus and atopic dermatitis

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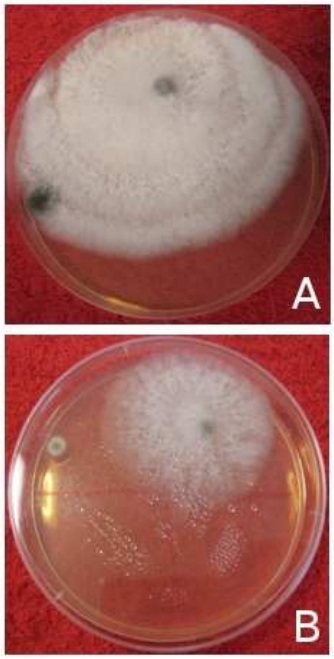

Figure 3. Petri dish with T mentagrophytes before and 3 days after LP Nd:YAG laser irradiation. Note the inhibition of growth in treated colonies.

Primary outcome measures:
Clinical improvement Time Frame: 12 months
Secondary outcome measures:
Mycological negative Time Frame: 3 months

Type of Onychomycosis	***Number of patients***
Total dystrophic	2
Distal subungual	7
Proximal subungual	3
Endonyx	2

Table 1. *Clinical types of fungal nail infection in treated group*

Special attention was paid to the possibility of factors which could cause additional nail pigmentation:

- nail polishes, which could contain magnesium or iron
- intake of isotretinoin or other antimycotic drugs
- long term use of griseofulvin or other cefalosporins, minocyclin
- local application of cytostatics (busulfan, 5-fluorouracil)
- professional exposure to dyes, asphalt …

The patients were asked to cease taking any vasodilators before treatment; these medications increase blood flow through the nail region (and thus enable quicker cooling).

Factors which contribute to fungal nail infections:

- diabetes
- professional exposure to sugar (cooks, confectionerists, candy makers, sportsmen,..)
- exposure to traumas (minor or maior trauma like subungual ematomas, …)
- activities contributing to excessive sweating of feet and skin maceration
- pedicure treatments

Prior to laser treatment, positive fungal cultures (Sabouraud peptone-glucose agar) were obtained from all patients, after direct microscopy, as a screening test. Scrapings were mounted for direct examination in 25% KOH mixed with 5% glycerol, heated (e.g., for 1 h at 51 to 54°C) to emulsify lipids, and examined under 3400x magnification for fungal structures.

Laser therapy was performed with 1064 nm Nd:YAG laser using the following parameters: 35 to 40 J/cm2 fluence, 25 ms pulse duration, 4 mm spot size, 1 Hz frequency.

Each nail was fully covered with a laser beam in a spiral pattern starting at the nail periphery and finishing in the nail centre (Fig. 2).

In one session three passes across each nail plate with two minutes pauses between passes were applied. The full treatment consisted of four sessions executed on days 0, 7, 14 and 21. Nails were photographed with a high resolution digital camera before treatment, immediately post treatment and at month 1, 3, 6 and 12.

In-vitro developed fungal cultures were also irradiated with laser beam until eradication (Fig. 3). Follow-up was performed at 3, 6 and 12 months, with mycological check-ups at 3 and 6 months.

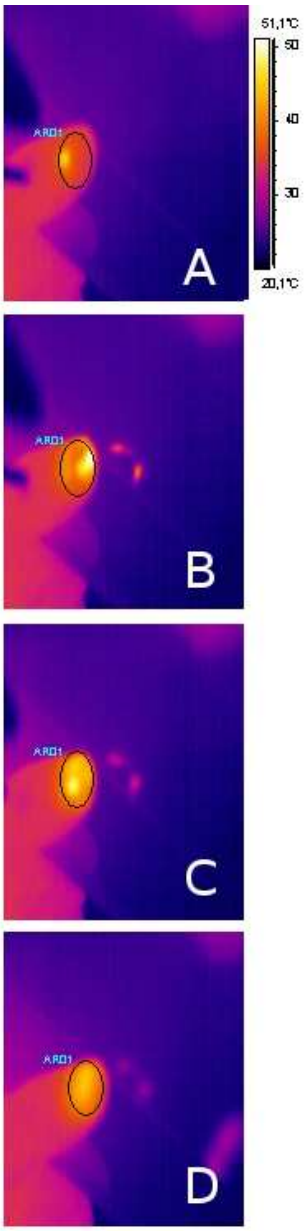

Figure 4. Laser scanning across the surface of the affected nail increases the temperature indside the nail plate

Fungal Isolate	*Number of Patients*
Candida sp	4
T. rubrum	6
T. mentagrophytes	1
Aspergilus niger	3

***Table 2**. Results of fungal nail isolates in a primary isolation medium Sabouraud peptone-glucose agar*

Temperatures achieved on the surface of irradiated nails were measured with thermal imager (Fig. 4).

RESULTS

Forty-two nails of 14 patients having clinically and mycologically proven onychomycosis, were submitted to transcutaneous laser irradiation with the aim of deactivation and eradication of fungal infection. Several cases are shown in Figures 1 and 6.

In 13 (93%) of the patients mycological clearance was observed at 3 months follow-up. In one patient with total dystrophyc type of onychomycosis a positive culture after 3 months from the first treatment procedure was repeated. After repeated treatment (4 sessions) in all 14 patients full clearance was achieved at 6 and 12 months.

Measurement of temperature on the nails during and after 1064 nm Nd:YAG scanning suggest that the nail is fully covered in approximately 15 sec, reaching cca 50°C and the cooling down phase below 40°C is usually longer than 1 minute (Fig. 5).

Besides for a mild to moderate heat sensation during the laser procedure, no other side effect were noticed. No complications were recorded. Final results were very satisfactory.

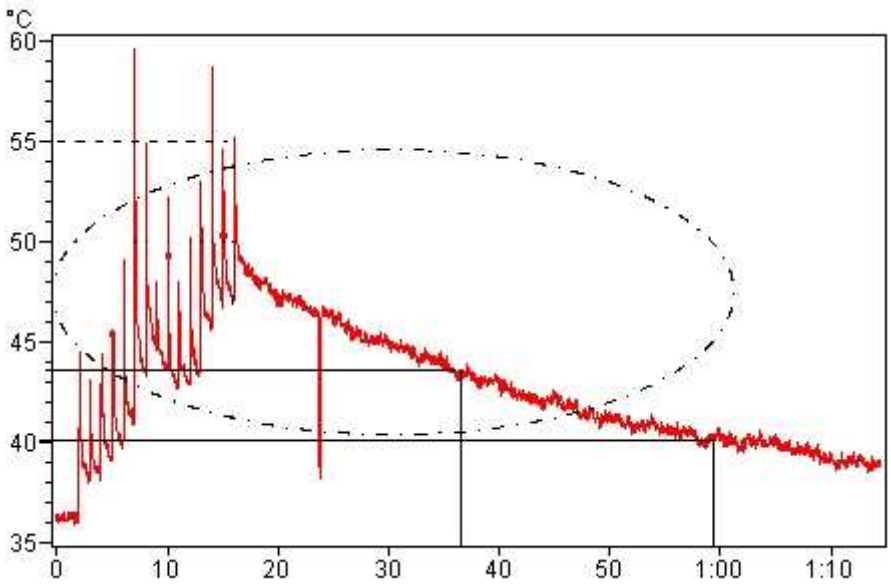

Figure 5. Measurement of nail temperature after Nd:YAG laser scanning. 40 J/cm^2 fluence, 25 ms pulsewidth, 4 mm spot size, 1 Hz frequency.

DISCUSSION

One of the main advantages of laser therapy is its bactericidal effect. Laser light causes local hyperthermia, destruction of pathogenic microorganisms, and stimulation of the reparative process (Ref. 1). Pathophysiology of laser irradiation show that the properties of laser beam deactivate the unwanted organisms by denaturing or partially denaturing one or more of the molecules within the pathogens. The beam accomplishes this by initiating a photobiological or photochemical reaction that attacks the pathogen cell or by inducing an immune response that attacks the organism.

Statistically significant growth inhibition of T.rubrum was detected in colonies treated with the 1064 nm Q-switched Nd:YAG laser at 4 and 8 J/cm2 (Ref.2). This laser produced significant inhibitory effects upon the fungal isolate T.rubrum in an in-vitro study. Meral, Tasar at al. reported high bactericidal effect on Candida albicans suspension after Nd:YAG laser irradiation (Ref.3). These findings suggest that, at a distinct energy level, the Nd:YAG laser has a higher bactericidal effect on small Candida populations.

Extracellular stress induces a heat shock response which involves induction of heat shock proteins (HSP) (Ref 4-9) The transmembrane yeast protein Wscl-Hcs77 acts as a heat shock sensor (Ref.10). Heat shock response is a natural way for cells to protect against environmental stress.

Dermatophyte fungi are characterized by their ability to grow in keratin and they adapt to their hosts in time. T.rubrum, which is a dermatophyte fungus, has a positive tropism towards oxygen. Apoptosis is cell death; it occurs in a regulated manner. Cell death results from an organized process involving an internal mechanism which typically includes fragmentation of the genome. Cells under stress either survive or succumb and die. The heat-response mechanism includes drastic repression of normal transcription and translation pathways and activation of a family of heat shock genes. If the stress is over the thermotolerance of the cell –as in this case, in which a physical stressor is applied– denatured proteins disrupt cellular homeostasis and increase reactive oxygen species (ROS) level. Severe protein denaturation leads to apoptosis of the fungal cell.

In one problematic case, a patient with total dystrophic onychomycosis tested positive three months from the first laser session. T.rubrum was isolated as the cause. Hyperkeratotic nail bed material was removed by a chemical agent. Reduction of hyperkeratosis and softening of the nail plate was achieved with 40% urea cream three days before the laser procedure.

CONCLUSION

This study evaluated and examined the inhibitory and direct effects of laser light on fungal tissue, fungal isolates, and omychomycotic nails. The proposed laser therapy is very effective in treatment of onychomycosis. We confirmed the disappearance of fungus by KOH and culture after a total of 4 irradiation sessions.

The reduction of nail bed hyperkeratosis before laser therapy is very important to achieve optimal results.

The procedure is simple and quick with no noticeable side effects or complications.

Figure 6 A,B,C,D,E. Results of long pulse 1064 nm Nd:YAG laser treatment of onychomycosis (A) Candida sp. before and after 6 months. (B) T.rubrum. before and after 3, 6 12 months. (C) Aspergilus niger. before and after 6 months.(D) T. mentagrophytes. before and after 6, 12 months.(E) Candida sp. before and after 3 months

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Jasmina Kozarev, MSc. has over fifteen years of experience in dermatology and skin disease treatment. She has performed over 2500 skin laser surgeries. Throughout her career Dr. Kozarev has gained a tremendous amount of experience using lasers on a daily basis. She has long-standing links with Fotona and has worked with many of the Fotona's laser systems in the aesthetic and surgery range and currently owns the SP Dualis. She is an expert lecturer with LAHA.