

Pharmacology and therapeutics

Combination of a triple wavelength (650 nm, 810 nm, and 915 nm) class IV laser system and local mechanical abrasion in the treatment of chronic toenail onychomycosis: an uncontrolled prospective pilot study

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Introduction

Onychomycosis is a persistent fungal infection of nails considered as a frequent dermatological disease, difficult to treat, especially in elderly patients or those with poor peripheral circulation.¹ The prevalence of onychomycosis is 5–18% in the adult population with a higher incidence in the industrialized countries.² In the central Alpine region of South Tyrol, the dermatophytes (*Trichophyton rubrum* and *Trichophyton interdigitale*) are the predominant pathogens with 53.3% of toenail onychomycosis followed by molds in 24.7% and yeast (usually *Candida*) in 22% of the cases.³ Any component of the nail may be involved,

Abstract

Background Toenail onychomycosis is a frequent fungal infection that is difficult to treat, especially in elderly patients. Diverse local and systemic antifungal treatments are available with variable results. Recently, different laser systems have been proposed for the treatment of onychomycosis, among them a class IV laser system adopting three different wavelengths, that is, 650, 810, and 915 nm (K-Laser Cube 3TM).

Objectives This prospective pilot study aims to clarify the clinical, histopathologic, and cultural mycological efficacy of the combination of a triple wavelength laser system and local mechanical abrasion in the treatment of toenail onychomycosis.

Methods Eight treatment sessions were performed involving a mechanical drill of the friable nail material followed by the laser treatment with four 2-minute cycles per nail with a median power of 3 W providing 240 J each. Clinical exam, mycological culture, and histopathology with PAS staining of nail clips were performed at the beginning and the end of the treatment period.

Results Nine patients with 16 clinically involved nails were included in this study (median age: 55.6). Clinical improvement was noted in eight patients (89%) at the end of the treatment cycles. Initial positive cultures could be reduced from six (67%) to two (22%), $P = 0.07$, while histopathologic examination by PAS staining remained invariable positive in all patients (100%).

Conclusion Despite clinical improvement, the combination of this laser treatment and mechanical abrasion could not reduce the fungal infection rate in affected toenails. Additional local or systemic antimycotic agents should be combined in order to avoid expected clinical recurrences.

including the nail matrix, nail bed, or nail plate; mostly it presents as distal-lateral subungual onychomycosis.⁴ Genetic predisposition, slow growth of the nail, reduced vascularization in the nail plate, and additional factors, such as occlusive footwear, frequent nail microtrauma, immobilization, or humid environment, can cause persistency and lack of success of treatment.⁵ Even if it is not a life-threatening condition, it may still lead to serious morbidity, including secondary bacterial infections, psychosocial, and emotional effects and may have an impact on quality of life.⁶

Diverse local and systemic antifungal treatments are available with variable treatment results. Before choosing a therapy,

several aspects have to be considered including patients' age, comorbidity, the severity of the penetration of the dermatophyte into the nail plate, and feasibility of local treatment by the patients or their caregivers. The percentage use of systemic treatment diminishes according to the patient's age group, whereas the use of topical treatment increases with the patient's age.³ Three main antifungal agents, namely itraconazole, terbinafine, and fluconazole, have been the gold standard in the treatment of onychomycosis for the last 2 decades.² The risk-benefit assessment has to be valued by every patient before starting systemic therapy due to common side effects including diarrhea, stomach upset, depression, taste or smell disturbances, and alteration of liver enzymes. Extra monitoring is required for toxicity or drug interactions.

Recently also different laser systems have been proposed for the treatment of onychomycosis due to their minimally invasive nature and the potential for requiring fewer treatment sessions,⁷ among them a class IV laser system adopting three different wavelengths, that is, 650, 810, and 915 nm (K-Laser Cube 3TM). This potential new treatment option offers the advantage of having few contraindications and minimal side effects. Moreover, it could allow to reduce patient monitoring and minimize the cost of systemic drug therapy. This prospective pilot study aimed to clarify if the proposed laser therapy would suffice as monotherapy if combined with local podologic mechanic abrasion in the treatment of chronic toenail onychomycosis.

Materials and methods

This study was performed at the South Tyrolean podologist center (Centro Podologico Altoatesino/Zentrum für Podologie, Südtirol, Bolzano/Bozen, Italy), being part of an evaluation of the standard treatment of the center. All patients signed an informed consent form before participation.

Eleven patients, three males and eight females, with a median age of 55 years, were enrolled in the study with a histologic, microbiologic, and clinical diagnosis of onychomycosis affecting at least one big toenail.

All the subjects confirmed not to use other topical, oral, light-based therapies, or photosensitizing systemic treatments. The main history was obtained as the duration of dystrophic nails, medical diseases, systemic treatments for other conditions, and sensibility to light. A clinical exam with photographic documentation, mycological culture, and histopathology with PAS staining of nail clips was performed at the beginning and the end of the treatment period.

Inclusion criteria were men and women older than 18 years of age with typical clinical onychomycosis, which was evident on at least one toenail of the hallux with positive PAS staining examination. Exclusion criteria were any usage of oral or topical antimetabolic therapy within the past 6 months, usage of photosensitizing systemic drugs during pregnancy, and the presence of other systemic diseases with possible nail deformity like psoriasis, lichen planus, or congenital nail disorders.

In total, eight treatment sessions were performed within a period of 28–44 days, approximately twice a week. The friable nail material from the affected nail was mechanically polished before the treatment, reducing the nail plate and with the aim to increase laser effectiveness due to deeper penetration of the laser into the layers of the nail. Mechanical abrasion was followed by laser treatment consisting of four sequential cycles each of 2 minutes per affected nail with a median power of 3 W providing 240 J each.

All subjects were asked to return after 1 month of treatment for the final follow-up and clinical evaluation. All the subjects were clinically evaluated, and mycological culture and histopathology with PAS staining of nail clips were performed. To evaluate the clinical efficacy of the laser treatment, high-quality photographs were taken. The outcome was evaluated by two independent investigators (KE and AEA) with a 4-point scale (no improvement –, slight improvement +, improvement ++, marked improvement/healing +++) before and after treatment. Clinical cure was defined as a clinically normal nail with a marked improvement from baseline to the final follow-up.

Results

In total, 11 patients (73% female) with onychomycosis (median age: 55 years) were treated with a class IV laser system adopting three different wavelengths, that is, 650, 810, and 915 nm (K-Laser Cube 3TM) adding local mechanical abrasion.

In total, eight treatment sessions were performed within a period of 28–44 days, approximately twice a week. The friable nail material from the affected nail was mechanically polished before the treatment, reducing the nail plate and with the aim to increase laser effectiveness due to deeper penetration of the laser into the layers of the nail. Mechanical abrasion was followed by laser treatment consisting of four sequential cycles each of 2 minutes per affected nail with a median power of 3 W providing 240 J each.

Nine patients completed the whole study and were successfully followed up through regular clinical consultations, and two participants removed themselves from the study, citing an unwillingness to continue follow-up examinations/photographs. Patients tolerated the procedures well with high satisfaction. None of our patients would discontinue the therapy due to pain or discomfort. The outcome data are represented in Table 1. Overall, eight of the nine participants (89%) had a positive clinical improvement at the end of the treatment cycles, one participant still had evidence of the dystrophic nail and showed no significant clinical improvement. Three patients (33.3%) showed clinical healing, and the remaining four patients (44.4%) showed evidence of partial clinical cure (decreasing area of dystrophic nail). Initial positive cultures could be reduced from 6 (67%) to 2 (22%), $P = 0.07$, whereas histopathologic examination by PAS staining remained positive in all patients (100%) (Figures 1–4).

Table 1 Summary of the pilot study including number of included patients, sex (M, male; F, female), age in years, outcome of the histologic exam with periodic acid Schiff (PAS) staining before and after the treatment period, cultural exam before and after the treatment period, the clinical outcome given as improvement (–, no improvement; +, slight improvement; ++, improvement; +++, marked improvement), and study duration in days

Patient number	Sex	Age	Histologic exam PAS nail clippings		Cultural exam		Clinical improvement	Duration (days)
			Before	After	Before	After		
1	F	55	+	+	<i>Aspergillus niger</i>	Negative	–	44
2	M	69	+	+	<i>T. mentagrophytes</i> and molds	Negative	+	42
3	M	59	+	+	<i>Candida</i> spp.	<i>Aspergillus niger</i>	+++	39
4	M	66	+	+	<i>T. mentagrophytes</i>	Negative	+	28
5	F	71	+	+	Negative	Negative	+	41
6	F	49	+	+	<i>T. rubrum</i> and <i>Aspergillus</i> spp.	<i>T. rubrum</i> and <i>Aspergillus</i> spp	+++	29
7	F	38	+	+	<i>T. mentagrophytes</i>	Negative	+	38
8	F	68	+	+	Negative	Negative	+++	36
9	F	54	+	+	Negative	Negative	++	33
10	F	40	+	n.d.	<i>T. rubrum</i> and <i>Aspergillus</i> spp.	n.d.	n.d.	n.d.
11	F	37	+	n.d.	<i>T. rubrum</i>	n.d.	n.d.	n.d.

T., Trichophyton; n.d., not done.



Figure 1 At the baseline (left) and clinical appearance (right) after eight triple wavelength (650, 810, and 915 nm) class IV laser system and local mechanical abrasion sessions within 39 days



Figure 3 At the baseline (left) and clinical appearance (right) after eight triple wavelength (650, 810, and 915 nm) class IV laser system and local mechanical abrasion sessions within 36 days



Figure 2 At the baseline (left) and clinical appearance (right) after eight triple wavelength (650, 810, and 915 nm) class IV laser system and local mechanical abrasion sessions within 36 days



Figure 4 At the baseline (left) and clinical appearance (right) after eight triple wavelength (650, 810, and 915 nm) class IV laser system and local mechanical abrasion sessions within 44 days

Discussion

In this pilot study, laser in combination with mechanical abrasion did provide positive clinical effects in the treatment of onychomycosis. Eight patients showed an improved nail, however, this did not correlate with mycological or complete cure, suggesting that the treatment of onychomycosis with a class IV laser system together with mechanical abrasion does not provide a mycological cure.

The fewer positive fungal cultures could be easily explained as an effect of the mechanical abrasion effectively decreasing fungal load from the nail, leaving less material for positive fungal culture.⁸

Also other treatment studies of laser did not show effects on fungal cure: A randomized, quadruple-blind, sham-controlled trial from Nijenhuis-Rosien et al.⁹ with 63 patients showed no significant differences in a complete and microbiological cure rate of onychomycosis between four treatment sessions (baseline and after 2, 4, and 12 weeks) with Nd-YAG laser (wavelength 1,064 nm, fluency 20 J/cm², spot size 3 mm, pulse rate of 5 Hz, power 10 W, and pulse duration 132 ms) and sham procedure in patients with diabetes. Before starting with (laser or sham) treatment, all affected nails were ground. Similarly, Tro Van Chau et al.¹⁰ used a fractional CO₂ laser in combination with a topical antifungal drug and compared it to oral itraconazole plus the topical antifungal drug. The authors reported that the laser group showed a significantly higher clinical improvement defined as a reduction in the mean SCIO at the end of the study compared with the itraconazole group ($P < 0.001$), though there were no significant differences between the laser and itraconazole group in the mycological clearance rate (73.3% vs. 79.1%).

The mechanisms of action of the laser for the treatment of onychomycosis are controversially discussed and are still uncertain. Some of the hypotheses already published are the heat fungicidal action over fungi, keratin proteins denaturation, the possible laser influence on cellular oxidative reactions, and changes in host immune modulation.^{11–14}

The results of this and other studies^{9,10} suggest that laser therapy is not effective in treating onychomycosis. Until now laser treatments have not kept their promises in onychomycosis treatment, and well-designed successful clinical trials are still missing. However, we cannot rule out that other laser devices, other wavelengths, or even a higher number of treatment sessions with shorter intervals could enhance microbiological cure.

Limitations

This study has some limitations. First, our sample size was small. The purpose was to examine the utility of a triple wavelength (650, 810, and 915 nm) class IV laser system in the treatment of chronic toenail onychomycosis that was intended to be used in a larger-scale study. As our original hypothesis could not be supported by the data, we had to renounce for

further testing. Second, follow-up duration was short, however, the mycological tests showed persistence of fungal infection after 1-month follow-up after several laser treatments and histopathologic examination by PAS staining remained highly positive in all patients (100%). The original hypothesis was that the laser would kill the fungal pathogen, but this was clearly not the case. For this reason, we believe that a longer follow-up would not have influenced the negative results.

Conclusion

Our original hypothesis that laser treatment in combination with mechanical abrasion would cure fungal onychomycosis via thermal or direct lethal effect through disruption of fungal vitality is not supported by the data. While the treatment did show clinical improvement, a mycological cure could not be reached. Additional local or systemic antimycotic agents should be added in order to avoid highly expected clinical recurrences.

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