A 1,320-nm Nd:YAG Laser for Improving the Appearance of Onychomycosis

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BACKGROUND Onychomycosis is a therapeutic challenge because of the toxicities of systemic medications. This has led to the investigation of light-based technologies for safe and effective alternative treatment modalities.

OBJECTIVE The purpose of this study was to determine the safety and efficacy of 4 treatments with a 1,320-nm neodymium:yttrium aluminum garnet (Nd:YAG) laser in improving the appearance of onychomycosis.

MATERIALS AND METHODS This study was a 24-week, single-center randomized placebo-controlled study. Ten subjects were enrolled with culture-proven, bilateral great toenail onychomycosis. The subjects received 4 treatments with the 1,320-nm Nd:YAG laser to the treatment toenail on Days 1, 7, 14, and 60. The control toenail received a sham treatment of cryogen cooling only. Mycologic cultures were obtained at 3-month follow-up visits.

RESULTS Fifty percent of mycologic cultures were negative at the 3-month follow-up after 4 laser treatments. Toenails had improvement in subungual debris, hypertrophy, and yellowing. Patient satisfaction was upheld as assessed by the Nail Quality of Life Questionnaire.

CONCLUSION The 1,320-nm Nd:YAG laser may be a safe and effective therapy for improving the appearance of onychomycosis. Additional therapy may be necessary to enhance long-term results. Further investigation needs to explore the optimal treatment settings and the most effective treatment schedule.

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Onychomycosis is a common fungal infection of the nails that affects approximately 1 in 10 Americans.[1] The most common pathogens are the dermatophytes, *Trichophyton rubrum* and *Trichophyton mentagrophytes*.[2] Other causative organisms include yeasts and nondermatophytic molds. Onychomycosis is often dismissed as a cosmetic concern. However, it is important to note that onychomycosis can become a source of more serious infections. Particularly in diabetics, onychomycosis may lead to ulceration, osteomyelitis, cellulitis, and ultimately tissue necrosis, which may rarely result in amputation.[3] There is no question that onychomycosis can significantly impact a patient's quality of life and warrants treatment.

Current treatment modalities have relatively limited long-term success. Topical antifungals are rarely effective because of their inability to penetrate through the nail plate, and recurrence often occurs after discontinuation of the medication.[4] Systemic options are the most effective treatment option. Oral terbinafine is currently the drug of choice.[5] However, potential adverse effects such as hepatotoxicity and drug interactions limit the use of systemic medications. Onychomycosis remains a treatment challenge

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because of a lack of safe and effective long-term treatment options. This has led to the investigation of laser-based treatments as an alternative therapeutic modality for onychomycosis.

Methods

This study was approved by the Institutional Review Board at the University of California, Irvine. Written informed consent was obtained from all subjects before enrollment. This is a single-center, randomized placebo-controlled study evaluating the efficacy and safety of a 1,320-nm long-pulsed neodymium: yttrium aluminum garnet (Nd:YAG) laser (CoolTouch CT3 Plus laser with CoolBreeze Zoom handpiece; CoolTouch, Roseville, CA) for improving the appearance of onychomycosis. Ten subjects with culture-proven, active bilateral great toenail onychomycosis, older than 18 years, were enrolled. Subjects were excluded if they were pregnant, had any other toenail disease (i.e., psoriasis), had excessively thick or hypertrophic nails, or were diabetic. Subjects on topical antifungals or systemic antifungals had to complete a minimum of a 2-week and 3-month exclusionary medicine washout period, respectively. Any surgical treatment required a 6-month washout period.

Great toenails were randomized to receive a 1,320-nm Nd:YAG laser treatment, and the alternate great toenail received a sham treatment with cryogen cooling only. All other toenails received laser treatments to prevent reinoculation from adjacent onychomycosis and were not included in graded assessments. Sham and laser treatments were performed on Days 1, 7, 14, and 60. Great toenails were treated with a 5-mm spot, 350-microsecond pulse width, 20 Hz, and 3 W at a target temperature of 38°C. The entire toenail was treated with the laser in a zigzag pattern until the target temperature was reached at which time the cryogen spray was delivered at 50 milliseconds. All other toenails were treated with a 3-mm spot at 1.5 W with the same target temperature and cooling. Additionally, both feet were treated with twice-daily application of an over-the-counter antifungal cream to prevent the spread of infection from adjacent tinea pedis.

On the days of treatment, digital photographs were taken. On follow-up Days 90 and 180, clinical evaluations, digital photography, and maximum linear clear nail growth (MLCNG) measurements were performed. The primary efficacy end point was improvement of the appearance of toenail onychomycosis as measured by MLCNG at 90 days compared with baseline. Secondary efficacy end points included clinical improvement of the degree of nail plate involvement (Table 1) and overall improvement (Table 2) based on the blinded assessment of clinical photography at 90 days compared with baseline (performed by 2 dermatologists who were not previously involved in the study); assessment of mycologic cure based on fungal cultures at 90 days compared with baseline; and subjective improvement of subject satisfaction based on the Nail Quality of Life Questionnaire at 90 days compared with baseline. Mycologic cure was determined by the fungal cultures of toenail clippings.

Results

Forty percent of treated nails had increased MLCNG. The average MLCNG for treated great toenails was 1 mm. Thirty percent of the control toenails had increased MLCNG. The average MLCNG for control toenails was 0.6 mm. Blinded assessment of the degree of nail involvement showed no change at 3 months compared with baseline for either the treated or control group. At 6 months, the treated toenails improved from an average rating of severe involvement (>67% involvement) to moderate involvement (34%–66% involvement) (Figures 1 and 2). The control toenails did not improve from an average rating of moderate involvement at 6 months compared with baseline. Blinded assessment of improvement in yellowing, subungual debris, hypertrophy, and overall appearance at 3 months showed minor (<25%) improvement in the treated great toenails compared with baseline. However, this was not significantly different from the control group. At 6 months, the overall improvement increased to a rating of minor to

TABLE 1. Grading Scale for Degree of Nail Involvement

<33%	Mild
34%–66%	Moderate
>67%	Severe

TABLE 2. Grading Scale for Overall Improvement	
0%	No improvement
<25%	Minor improvement
25%–50%	Minor to moderate improvement
50%–75%	Moderate improvement
>75%	Marked improvement

moderate (25%–50%) improvement. Similarly, this was not significantly different from the control group.

Fifty percent of mycologic cultures were negative at a 3-month follow-up for the treated great toenails. Interestingly, 70% of cultures were negative for the control group.

Patient self-assessment with the Nail Quality of Life Questionnaire determined that patient satisfaction was upheld. In reference to the treated toenails, subjects were less self-conscious less often. They felt less attractive less often and were less embarrassed. However, there was no significant difference from the control toenails.

Conclusion

Initial investigations for the laser treatment of onychomycosis were conducted with a 1,064-nm Nd:YAG laser such as the PinPointe FootLaser (NuvoLase, Inc., Chico, CA). Approximately 51% to 53% improvement in onychomycosis was seen at 24 weeks after 4 to 8 treatments.[6] However, the definition of "improvement" was not clarified. Other short-pulsed (JOULE ClearSense [Sciton, Inc., Palo Alto, CA][7]; GenesisPlus [Cutera, Inc., Brisbane, CA][8]) and long-pulsed (Fotona Dualis SP, Fotona, Slovenia)[9,10] 1,064-nm Nd:YAG laser systems have since been investigated for the treatment of onychomycosis. Although these studies show encouraging results, the studies are often unclear about what criteria are used to define cure. The 1,320-nm Nd:YAG laser has the potential to penetrate deeper into the nail plate compared with shorter wavelengths such as 1,064 nm. Hypothetically, this may result in more effective heating of the nail plate. However, greater improvement of onychomycosis from deeper light penetration is yet to be elucidated.

The exact mechanism of action of the 1,320-nm Nd:YAG laser for improving the appearance of onychomycosis is largely unknown. It is speculated that the laser denatures the pathogen through heat generation both selectively by targeting water in the hyphae and nonselectively through bulk heating. Water is present within the dermatophyte but is also abundant in collagen, and thus it is difficult to selectively target the hyphae.

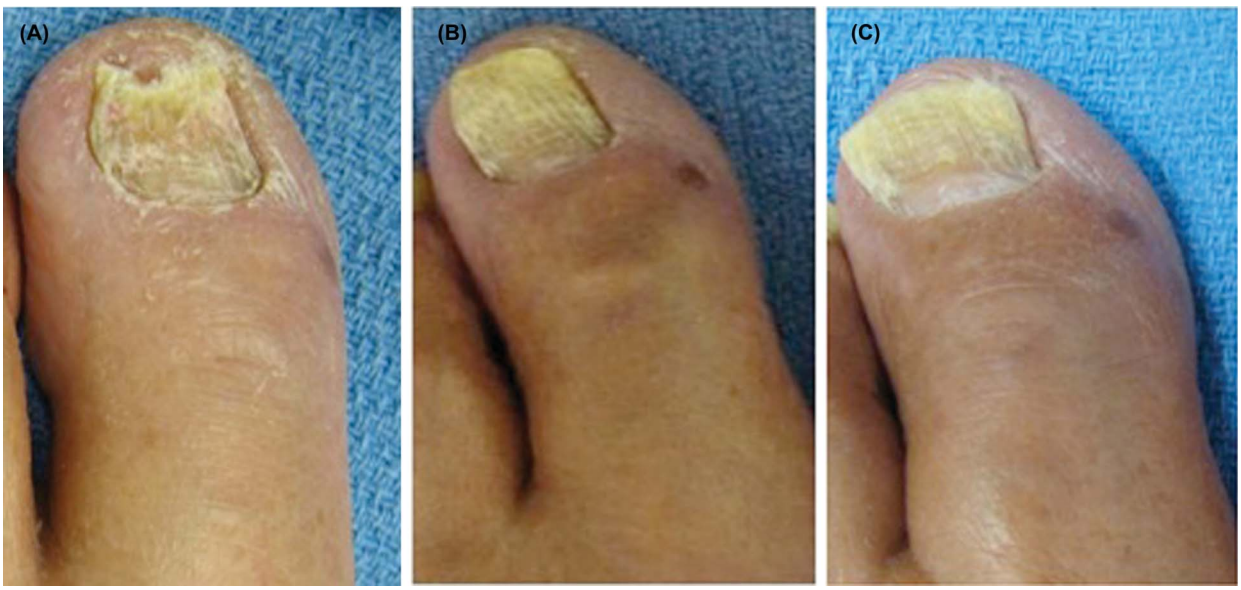

Figure 1. (A) Onychomycosis of the great toenail before laser therapy. (B) Three months after 4 laser treatments. (C) Six months after 4 laser treatments. Note the MLCNG improvement.

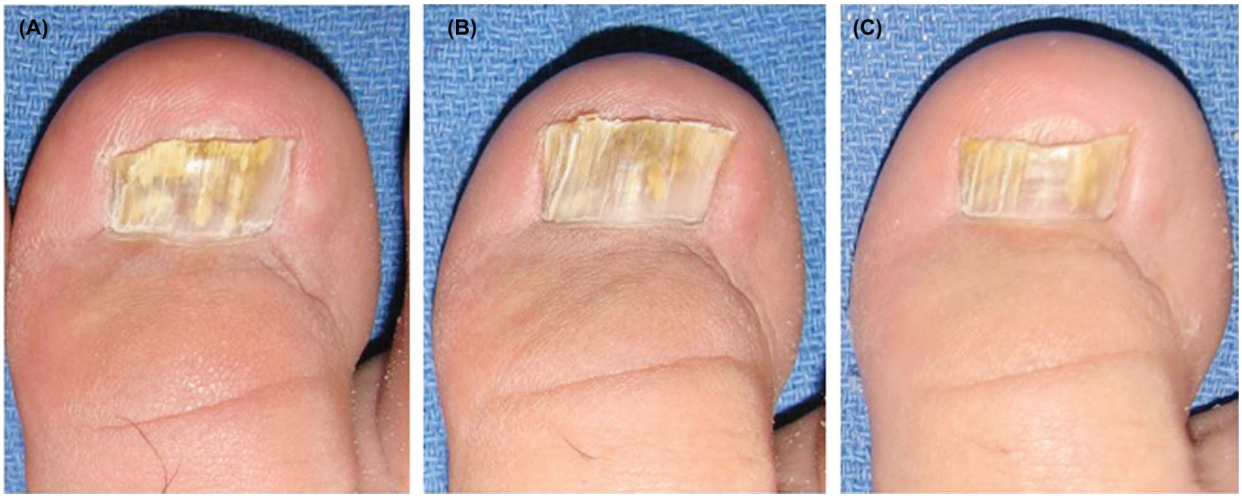

Figure 2. (A) Onychomycosis of the great toenail before laser therapy. (B) Three months after 4 laser treatments. (C) Six months after 4 laser treatments.

Regarding bulk heating, it has been shown that a temperature of at least 55°C for 5 minutes is required to kill dermatophytes in water suspension.[11] However, damage to normal collagen is seen at temperatures >45°C, and skin necrosis can be seen at 50°C.[12–14] Therefore, a mechanism of action based solely on nonspecific bulk heating of the dermatophyte would be at a high risk of destroying the surrounding normal tissue at temperatures high enough to eradicate the dermatophyte. Given the somewhat promising early results of this study, alternatively one can speculate that the heating of the host tissue may function by improving circulation in the area, possibly leading to a greater host response.

In retrospect, the authors consider that the topical antifungal may have confounded the study given that 70% of cultures were negative in the control toenails. The purpose of the antifungal was to prevent reinfection from tinea pedis. The authors did not anticipate observing any improvement in onychomycosis, given the poor penetration of topical antifungals into the nail plate. However, the improvement seen in the control group with topical antifungal monotherapy may be due to strict compliance of twice-daily application as instructed by the study protocol compared with real-life situations. An alternative explanation for the improvement seen in this group may have been due to a cooling effect from the cryogen spray sham treatment, which could have potentially destroyed the dermatophytes with freezing temperatures. Any further investigation of the 1,320-nm Nd:YAG laser for improving the appearance of onychomycosis should be conducted without any topical antifungal to avoid any influence on the data, because the authors do not know what effect this had on their results.

In conclusion, the 1,320-nm Nd:YAG laser may be a safe alternative therapy option for improving the appearance of onychomycosis. No serious complication was noted. Treatments were well tolerated, and patient satisfaction was upheld. The improvement that the authors observed may have been fungistatic rather than fungicidal because of extreme target temperatures necessary for destruction of the dermatophyte without the destruction of normal tissue. This underscores the importance of selective photothermolysis of more specific targets within the dermatophyte to spare surrounding skin structures. Otherwise, more treatments may be required for maintenance. Future investigation should aim to determine the optimal number of treatments, treatment schedule, wavelength, and pulse duration necessary for long-term efficacy.

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