Long-term treatment within a maximum of 96 weeks of tinea unguium with long-pulsed neodymium-doped yttrium aluminum garnet laser

Utako Kimura, Masataro Hiruma , Yasushi Suga
Departments of Dermatology, Juntendo University Urayasu Hospital,
Urayasu City, Chiba, Japan

Introduction :

Onychomycosis (tinea unguium) is a relatively common fungal nail infection that causes nail turbidity, trachyonychia, discoloration, and brittleness. Twelve million individuals in Japan are estimated to have tinea unguium.[1] This is consistent with the reported incidence of onychomycosis in the United States (US) which ranges from 14%[2] to 28% in persons over 60 years of age.[3] Although oral and topical antifungal medications are currently the first line of treatment for onychomycosis,[4] their efficacy is limited. The efficacy of oral antifungals ranges from 14% to 50% [5, 6] with the recurrence (relapse or reinfection) rate of 10% to 53%.[5] On the other hand, the efficacy of topical medications is between 5.5% and 8.5% due to their inability to fully penetrate the nail bed.[7-11] Alternative treatment options include mechanical avulsion of the infected toenail by clips or grinder,[12] chemical avulsion by morpholine salicylate and uric acid or a combination ointment.[13] Surgery, while effective, is rarely used as it causes undue pain and may lead to post-operative complications, especially in diabetic or immunocompromised patients.

Background :

Advancements in laser technology have resulted in effective treatments of onychomycosis with relatively minimal patient discomfort. In recent years, several studies have been conducted on a new treatment using a long-pulsed 1,064nm neodymium-doped yttrium aluminum garnet (LP-Nd:YAG) laser, which is much less invasive than conventional treatments with oral medications. We examined the long-term efficacy and the safety of the LP-Nd:YAG 1,064nm laser in treating Onychomycosis during a maximum of 96-week follow up period.

Objectives :

Evaluating long-term efficacy and safety of using the LP-Nd:YAG laser (Xeo™, Cutera Inc., Brisbane, CA, USA) for tinea unguium follow up period within a maximum of 96 weeks.

Subjects :

- 46 patients visited our outpatient department for treatment of tinea unguium (total 100 toes) .
- 21 male and 25 female, with a mean age of 68.8 years old and mean disease duration of 12.6 years.
- All subjects were resistant to oral medication or had difficulty in taking medications.
- All subjects showed nail plate opacity and tested positive for fungus on direct microscopic examination using a KOH preparation.
- Treatment history with topical anti-fungal agents: 40 subjects out of 46 subjects.
- Treatment history with oral anti-fungal agents: 10 subjects out of 46 subjects.

Exclusion criteria :

- Medical history of using an oral antifungal medication within a half year.
- Medical history of using a topical antifungal medication within a week.
- Serious disease that affects the entire body.
- A chance of pregnancy.
- Bleeding tendency.

Laser Treatment Settings :

- Spot Size: 5mm
- Pulse Width: 0.3msec (300μs)
- Fluence: 14J/cm²
- Repetition Rate : 5Hz
- Number of Pulses
  - A great toe received 100 to 200 pulses
  - The second to fifth toes received 20 to 100 pulses each
- Treatment Interval: 4 weeks ± 1week

Figure 1. Hand piece was held 1cm to 2cm off the toenail surface.

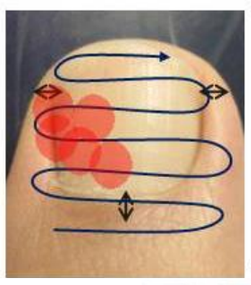


Figure 2. Infected nail area was irradiated extending 2mm over the medial and lateral nail fold and 4mm over the proximal nail fold.

Patient Evaluation (Degree of Improvement) :

Turbidity Assessment

- Degree of turbidity was determined using a turbidity scale (ranging from "0 = clear nail" to "10 = completely turbid nail") at each visit.
- Turbidity scores were calculated using the formula (1-X/Y) × 10 (Figure 3) where X (mm) represents the clear nail length and Y (mm) is the total length of the toenail.
- Improvement in turbidity was determined by comparison of turbidity scores at baseline and 24, 48, 72 and 92 weeks.

Overall Improvement

- Treatment efficacy was assessed by an overall improvement scale (0 to 4) which combined improvement in turbidity scores and microscopic examination. Overall improvement was classified as "4 = complete clearance" if the turbidity score indicated "0 = clear nail" accompanied by a negative microscopic result. No microscopic examination was performed unless the turbidity score showed "0 = clear nail".

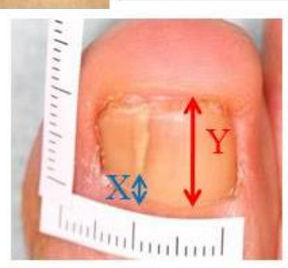


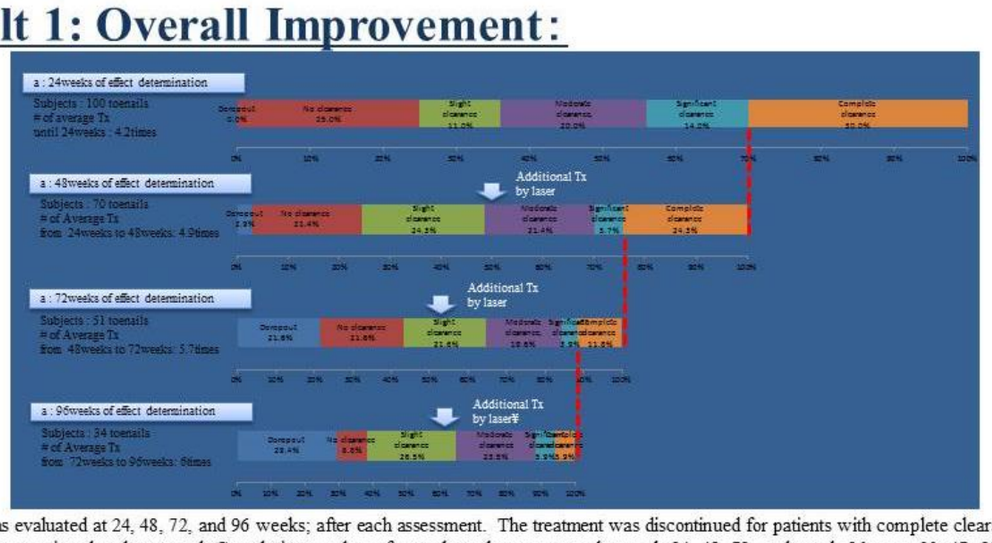
Figure 3.
Calculation of turbidity score of the infected area = (1-X/Y) × 10
X = Length of uninfected toenail growth proximal to turbidity
Y = Total length of toenail

Patient Evaluation (Photograph) :

Standardized photographs were taken at baseline and at each 4 week visits using a digital single-lens reflex (SLR) camera (EOS7D, Canon K.K., Tokyo, Japan).

Efficacy was evaluated at 24, 48, 72, and 96 weeks; after each assessment, treatment was discontinued for healed patients, whereas patients who were not healed continued to be treated.

Result 1: Overall Improvement :



Efficacy was evaluated at 24, 48, 72, and 96 weeks; after each assessment. The treatment was discontinued for patients with complete clearance, otherwise patients were continued to be treated. Cumulative number of complete clearance toes by week 24, 48, 72, and week 96 were 30, 47, 53, and 55 toes, respectively. 47 toes (85%) out of the 55 complete clearance toes eventually healed by week 48, however this number did not increase with same tendency after week 72 follow up.

Result 2: The improvement ration by mycosis type at week 24

			Species causing onychomycosis			Total
			T.rubrum	T.mentagraphytes	Unexamined / nonidentifiable	
Improvement rate of turbidity	Complete clearance	Number of toes	13	2	15	30
		%	24.5%	18.2%	41.7%	30.0%
	Significant clearance	Number of toes	4	2	8	14
		%	7.5%	18.2%	22.2%	14.0%
	Moderate clearance	Number of toes	11	2	7	20
		%	20.8%	18.2%	19.4%	20.0%
	Slight clearance	Number of toes	9	1	1	11
		%	17.0%	9.1%	2.8%	11.0%
	No clearance	Number of toes	16	4	5	25
		%	30.2%	36.4%	13.9%	25.0%
Total		Number of toes	53	11	36	100
		%	100.0%	100.0%	100.0%	100.0%

Result 3: The improvement ration by onychomycosis type at week 24

			Types of Onychomycosis				Total
			DLSO	SWO	PSO	TDO	
Improvement rate of turbidity	Complete clearance	Number of toes	26	2	0	2	30
		%	34.7%	33.3%	0.0%	11.8%	30.0%
	Significant clearance	Number of toes	9	2	0	3	14
		%	12.0%	33.3%	0.0%	17.6%	14.0%
	Moderate clearance	Number of toes	17	1	1	1	20
		%	22.7%	16.7%	50.0%	5.9%	20.0%
	Slight clearance	Number of toes	8	1	0	2	11
		%	10.7%	16.7%	0.0%	11.8%	11.0%
	No clearance	Number of toes	15	0	1	9	25
		%	20.0%	0.0%	50.0%	52.9%	25.0%
合計		Number of toes	75	6	2	17	100
		%	100.0%	100.0%	100.0%	100.0%	100.0%

Result: case 1, 79 yo, female, DLSO

4 weeks interval, 6 Laser Tx

Discussion 1 :

- This study reports our clinical experience with the LP-Nd:YAG 1,064 nm laser in treating onychomycosis of varying severity in 100 affected toenails of 46 subjects. All patients enrolled in this study had a prior history of ineffective oral and topical antifungal medication use.
- For effectiveness and safety, even though no subjects had combination therapy using an antifungal agent, LP-Nd:YAG procedure showed 64%, moderate to complete clearance, improvement in the follow-up of up to 24 weeks. Also 55% of infected toenails showed complete clearance within the 96-week study period. In addition, there are no severe side effects occurred.
- Although the mechanism of action of lasers in treating onychomycosis is still unknown, effectiveness is thought to result from bulk heating to thick horny cell layer and internal nail harboring the fungus which is a weak pathogen that is susceptible to heat. Hypothetically, the laser generated heat suppresses the growth of fungus colony. In addition, particular features of the laser wavelength or heating effects may stimulate infected nails to promote more rapid nail growth.
- Instead of terminating the treatment several times, it is better to keep continue the treatment until the infected nail get complete turbid at least up to 48 weeks since up to 48 weeks, it is likely to lead to healing. However, in the treatment continues for over 48 weeks, the ratio of complete heal was a gradually reduced. Therefore, if there is no change observed at the week 48, either choosing other therapies and/or combination therapy may be considered.

Conclusion :

- The preliminary results of this study show that this treatment modality is safe and effective for the treatment of onychomycosis in the long-term.
- Additional studies are needed to more fully assess the clinical and mycological benefits as well as optimize the treatment protocol and parameters.
- Thus, although laser treatment alone may be effective in about half of the affected toes, combination with other treatments should be considered if no improvement is seen after 48 weeks (approximately 1 year). We will continue an effort to optimize the treatment protocol and parameters for providing better performance of this therapeutic method.