Long-Pulsed Nd:YAG (1064nm) Laser Versus Q-Switched Nd:YAG (1064nm) Laser for Treatment of Onychomycosis

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Background and Objectives: To compare the efficacy of the long-pulsed Nd:YAG (1064nm) laser versus the Q-Switched Nd:YAG (1064nm) laser in treatment of onychomycosis.

Study Design/Materials and Methods: This is a prospective cohort study. It was carried out on 20 patients with clinical and mycological evidence of onychomycosis who were randomly assigned into two groups; group I: included 10 patients treated with biweekly sessions of long-pulsed Nd:YAG (1064nm) laser and group II; included 10 patients treated with monthly sessions of Q-Switched Nd:YAG (1064nm) laser. The assessment was done using proximal nail measurement and microscopic examination using 10-20% potassium hydroxide solution and culture on Sabouraud's dextrose agar. All patients were followed up for 6 months after the last treatment session.

Results: Fungal isolates in the present study were grouped into yeast in 50%, non-dermatophyte moulds in 10%, while dermatophyte infection was detected in 40%. Each group showed a statistically significant improvement in proximal nail plate measurements with no statistically significant difference between both groups. Mycological cure was only achieved in 40% of group I and 50% of group II. Patient satisfaction was higher in group II.

Conclusions: Both long-pulsed Nd:YAG (1064nm) and Q-Switched Nd:YAG(1064nm) laser systems can be used as a safe and effective modality in the treatment of onychomycosis, particularly in patients who refuse or have a contraindication to oral antifungal treatment. Lasers Surg. Med. 00:00-00, 2019. © 2019 Wiley Periodicals , Inc.

Key Words: onychomycosis; laser; Nd:YAG laser

INTRODUCTION

Onychomycosis affects approximately 5% of the population all over the world and its incidence is increasing because of many factors such as immunosuppression, diabetes, and advancing age {1,2]. It accounts for one third of all fungal skin infections [3] and up to 50% of all nail diseases [4]. Dermatophytes are the most common cause of onychomycosis. However, non-dermatophytic moulds are becoming more common worldwide. In addition, onychomycosis due to Candida is prevalent but not so common [5].

The primary aim of treatment is to eradicate the organism as demonstrated microscopically and by culture, this is defined as the primary endpoint. Clinical improvement and cure are secondary endpoints [6]. Also, important points are to reduce its morbidity and to prevent complications [7].

The use of lasers to treat nail fungus is not new. Researchers have been using lasers to treat onychomycosis since the 1980's [8].

Most of these lasers depend on delivering a concentration of laser energy in a small area to penetrate deeper into the nail plate. The mechanism of the effect of laser light on fungal cultures in vitro and in vivo is controversially discussed and is still uncertain at this point [9]. As fungi are heat sensitive above 42°C, absorption of laser energy results in sustained photothermal heating of the mycelium causing it fungicidal effects. However, heating dermal tissue to temperatures above 40°C results in pain and necrosis; therefore the laser energy must either be pulsed to allow the dissipation of heat by the tissue or delivered at a moderate level to prevent subsequent tissue damage [10,11].

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MATERIALS AND METHODS

This study was carried out on twenty patients with clinical and mycological diagnosis or onychomycosis, who were divided randomly into two groups; group I included 10 patients treated with biweekly sessions of long-pulsed 1062nm Nd:YAG laser and group II included 10 patients treated with monthly sessions of Q-switched 1062nm Nd:YAG laser. This study excluded patients with concomitant nail disorders (psoriasis, atopic dermatitis, lichen planus etc.), patients who used systemic antifungal within 6 months of the first scheduled laser session and pregnant women, Patients of both groups received a minimum of five sessions and were followed up for 6 months after the last session. Informed consent was taken from all patients.

All patients were subjected to:

(1) History taking: regarding durations of lesions, previous treatments, response to treatment and other medical conditions.

(2) General and dermatological clinical examination to exclude skin diseases with associated nail disorders.

(3) Clinical assessment of onychomycosis including the number of nails affected, site (finger, toes, or both) and type.

(4) Proximal nail plate measurement at baseline, in every session, at the end of the sessions and after a 6-month follow-up.

(5) Mycological examination by direct microscopy and mycological culture done at baseline (before treatment), at end of the sessions and 6 months after the last treatment (at the end of the follow-up period).

The nail of the patient was first disinfected by 70% alcohol using a piece of sterile gauze to reduce contamination. The nail specimens were collected by nail clippings, nail scrapings or subungual curettage, then the specimen was taken in a sterile plastic Petri dish.

The nail specimen was divided into three parts for microscopic examination (with potassium hydroxide 10–20% added) and culture on Sabouraud dextrose agar medium (SDA) with chloramphenicol and Sabouraud's dextrose agar with cyclohexamide and chloramphenicol (SDA + C + C).

Cultures were incubated at 25°C under aerobic conditions and observed for growth for a period of 2 weeks but whenever no growth in the tubes was observed, the period was extended up to 1 month.

(6) Digital photography: nails were photographed with a high-resolution digital camera at day 0 (pre-treatment photograph), before every session and at the end of the follow-up period at 6 months using the same camera settings.

(7) Laser sessions. Topical anesthesia using EMLA® 5% cream (lidocaine 2.5% and prilocaine 2.5%) under occlusion at least 1 hour prior to the session.

Ten patients received a long-pulsed 1,064-nm Nd:YAG laser session every 2 weeks using an Apogee Elite® Laser System (Cynosure Co. Westford, MA) with the following parameters: fluence: 35 J/cm2, pulse duration: 25 milliseconds, spot size: 5 mm, frequency: 1 Hz and the cooling system was stopped.

Ten patients were treated with Q-Switched 1,064 nm Nd:YAG laser every 4 weeks using COSJET-TR® Q-switched Nd:YAG Laser (WON technology Co., South Korea) with the following parameters: fluence: 14 J/cm2, spot size: 3 mm, frequency: 5 Hz.

Two passes were done with a 1-minute interval in both types of laser. There was no identifiable endpoint for long-pulsed Nd:YAG. On the contrary, we noticed immediate clearance of chromoychia in some patients treated with Q-switched Nd:YAG with the characteristic cracking sound. Pain during the sessions was assessed on a scale from 0 to 10.

Clinical assessment of the target nail was performed by means of the following parameters; we compared clinical response at end of therapy and after 6-month follow-up with baseline and classified the response as follows: [1] cure: the nail was clinically normal, and healthy nail regrowth was complete [2]; improvement: healthy nail plate was greater than at baseline, but nail regrowth was incomplete [3]; failure: no clinical improvement was observed or recurrence at the follow-up period.

RESULTS

Demographic data of both groups are shown in Table 1. The duration of the disease among patients ranged from 1 month to 5 years, there was no statistical

TABLE 1. Comparison Between the Two Studied Groups According to Demographic Data

	Long-Pulsed (*n*=10)		Q-Switched (*n*=10)			
	No.	%	No.	%	Test of sig.	*P*
Sex						
Male	1	10.0	2	20.0	X^2=0.392	^{FE}P=1.000
Female	9	90.0	8	80.0		
Age						
Min.-Max	16.0-58.0		31.0-57.0		*t*=1.316	0.205
Mean +- SD	38.70 ± 14.0		45.60 ± 8.88			
Median	36.50		47.0			
Residence						
Urban	8	80.0	5	50.0	X^2=1.978	^{FE}P=0.350
Rural	2	20.0	5	50.0		
Occupation						
Handy Worker	2	20.0	3	30.0	X^2=1.304	^{MC}P=0.695
Housewife	5	50.0	6	60.0		
Academic Work	3	30.0	1	10.0		

χ2, χ2, and P values for χ2 test for comparing between the two groups.

^{MC}P: *P* value for Monte Carlo for χ2 test for comparing between the two groups.

^{FE}P: *P* value for Fisher Exact for χ2 test for comparing between the two groups.

t, *P*: *t* and *P* values for Student's *t* test for comparing between the two groups.

significance difference between the two studied groups as regards the duration of the disease.

Regarding the number of affected nails; patients were categorized into five groups as follows; single toe nail, single fingernail, multiple toe nails, multiple fingernails and finally multiple both toe and fingernails. There was no statistically significant difference between both studied groups as regards these categories. The total number of nails treated was 120 nails (50 nails in group I and 70 nails in group II).

The clinical types of onychomycosis were as follows; eight patients (40%) with total dystrophic onychomycosis and 12 patients (60%) with distal and lateral subungual onychomycosis equally presented in the two groups.

Nail cultures at baseline revealed that Candida was the most commonly isolated organism (50% of cases) followed by dermatophytes in 40% (25% Trichophyton mentagrophyte and 15% Trichophyton rubrum) and aspergillus in 10%. There was no statistically significant difference between both groups as regards the isolated fungi.

At the end of the sessions; mycological clearance was achieved only in 40% in group I and 30% in group II

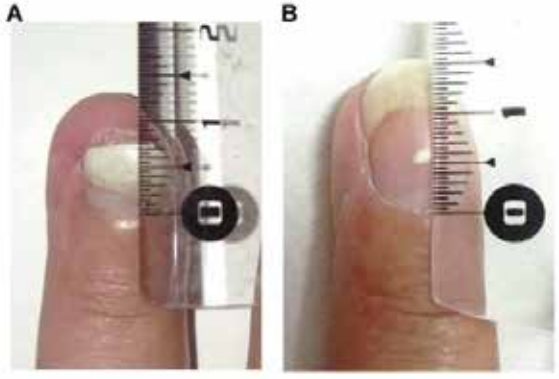

Fig. 1. Right index fingernail before treatment (**A**) with long-pulsed Nd:YAG 1,064 nm and at the end of the follow-up period (**B**). Proximal nail plate measurement is significantly increased showing a complete clinical cure. [Color figure can be viewed at wileyonlinelibrary.com].

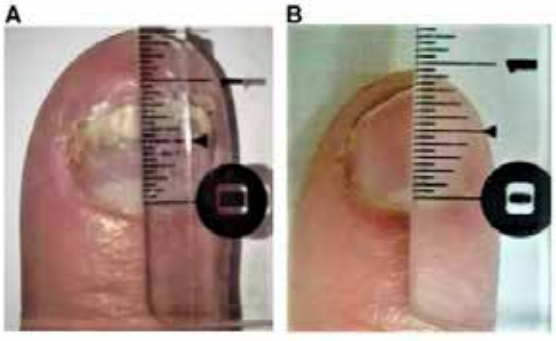

Fig. 2. Left index fingernail before treatment (**A**) with long-pulsed Nd:YAG 1,064 nm and at the end of the follow-up period (**B**). Proximal nail plate measurement is significantly increased showing a complete clinical cure. [Color figure can be viewed at wileyonlinelibrary.com].

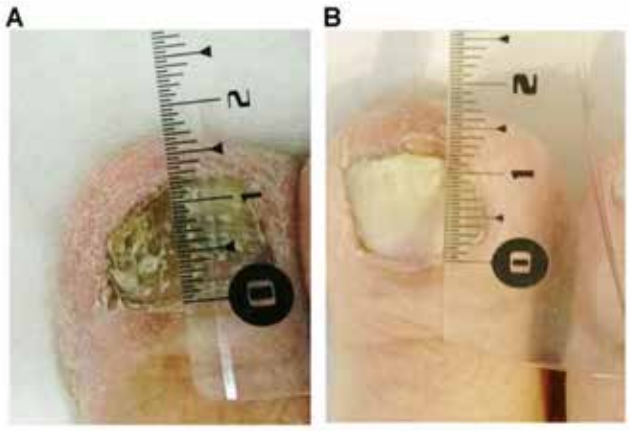

Fig. 3. Right big toenail before treatment (**A**) with Q-switched Nd:YAG 1,064 nm and at the end of the follow-up period (**B**). Proximal nail plate measurement is significantly increased showing a complete clinical cure. [Color figure can be viewed at wileyonlinelibrary.com].

with no statistically significant difference between both groups. The same result was detected at the end of the follow-up period regarding group I while it was increased in group II up to 50% achieving a statistically significant improvement.

We noticed that nails infected with yeast showed more improvement, but it was not statistically significant. This may be attributed to the finding that yeast was the most common fungi isolated in both groups.

The present study revealed a non-significant relation between the mycological response at the end of the session and both types of fungus in culture media and clinical types of onychomycosis in both groups.

Comparison of proximal nail plate measurements at baseline and end of the sessions showed a statistically significant improvement in both groups (P = 0.018, 0.007, respectively) but with no statistically significant difference between them. The means of proximal nail plate measurements after 6 months were significantly increased in both groups in comparison to the baseline and end of session measurements but there was still no statistically significant difference between them.

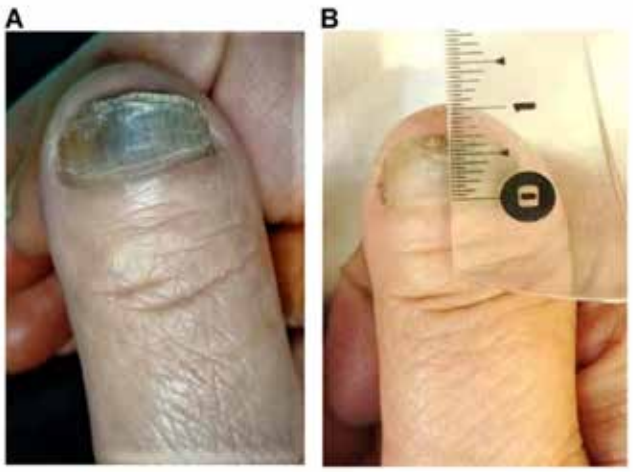

Fig. 4. Right thumb fingernail before treatment (**A**) with Q-switched Nd:YAG 1,064 nm and at the end of the follow-up period (**B**). Proximal nail plate measurement is significantly increased showing clinical improvement and clearance of chromonychia. [Color figure can be viewed at wileyonlinelibrary.com].

Comparison between the two studied groups according to clinical assessment at the end of sessions showed the following; group I showed a clinical success in 70% of patients (four patients cured and three patients improved) (Figs. 1 and 2), and failure was detected in three patients (30%). On the contrary, group II showed a clinical success in 90% of patients (three patients cured and six improved) (Figs. 3 and 4), and failure was detected only in one patient (10%). Clinical success was statistically significant in both groups with no statistically significant difference between them. The total number of treated nails was 120 nails; clinical success was achieved in 98 nails with failure in 22 nails. We noticed that fingernails had achieved more response than toenails at the end of the follow-up period, but it was not statistically significant. This finding may be attributed to the faster rate of fingernail growth in comparison to toenails.

On the comparison between the two studied groups according to clinical assessment at the end of the follow- up period; clinical success was upgraded to 80% in group I with 20% failure (one patient with no response and recurrence after clinical cure in another one). Group II was exactly the same as at the end of the sessions. Clinical success was statistically significant in both groups with no statistically significant difference between them.

Mild to moderate pain sensation was the most common side effect of treatment in both groups, it was relatively higher in group I but not to a statistically significant level. Nail discoloration, slow growth, and acute paronychia were also reported by some patients, but not statistically significant.

Patient's satisfaction was higher in group II but with no statistically significant difference between both groups. It was assessed on a scale from 0 to 10, and we think it was related to lower pain scores together with less frequent sessions.

DISCUSSION

The present study revealed that the age of patients rangedfrom 18 to 54 in both groups with a mean age of 38.7 (±14.0)years in group I and 45.6 (±8.88) years in group II. It iscommonly reported that onychomycosis prevalence increases with age ranging between 40 and 60 years old [12,13].

The present study reported that onychomycosis was more common in females than males in a ratio of 9:1 in group I and 8:2 in group II.

A female predominance was also reported in many studies, such as those by Bramono et al. This can be attributed to the fact that females are involved in household wet work like laundry and house cleaning, they are also more concerned about their cosmetic appearance than males [14–16].

In the present study, onychomycosis was more commonin patients living in urban areas (65%) compared with those living in rural areas (35%). This was in accordance with a study by Kaur et al., documenting that 85% of their patients lived in urban areas, and 15% lived in rural areas. This can be related to the higher socio economic class in the urban community and better medical services. Our results were in contrast to another study by Jesudanam et al., which showed that 94.12% of their patients lived in rural areas [17,18].

According to this study, onychomycosis was more common in housewives (50%, 60%, respectively) which matches with the study of Jesudanam et al. [18] Females (specially housewives) are more exposed to household activities like cleaning, washing, etc. Subsequently, their hands and feet are more immersed in water, detergents and chemicals, therefore they are more liable to nail trauma. In the present study, distal–lateral subungual onychomycosis was the most common type (60%) followed by total dystrophic onychomycosis (40%). This was confirmed by Matos et al. [19] and Araújo et al. [20] studies that showed distal and lateral subungual onychomycosis (62.5%) being the most prevalent followed by (20.8%) with proximal subungual infection and (12.5%) with total dystrophic onychomycosis. Our results are in accordance with the results recorded by other studies by Sujathaet al. [21] and Veer et al. [22]. The fungal isolates showed that yeast infection was the most common (50%) mainly Candida species followed by dermatophyte infection(T. mentagrophyte and T. rubrum) (40%) and with nondermatophyte moulds in 10% (Aspergellus flavus). In contrast, the studies of Kaur et al. [17], Matos et al. [19], and Sujatha et al. [21] showed that dermatophytes mainly T. rubrum were the most prevalent followed by yeast. In agreement with our results; Godoy et al. [23] showed that Candida species were the most common agents in finger-nail onychomycosis (38.3%), dermatophytes did play amajor role in fungal infection of toenails onychomycosis (31.6%).

Patients were assessed both at the end of the sessions and at the end of the follow- up period (6 months). Assessment was done clinically, mycologicaly, photographically and by proximal nail fold measurements.

In the first follow-up after end of the session, the results revealed mycological clearance by culture in (40%) in group I and 30% in group II while most of the patients were still mycologicaly positive.

These results are in agreement with another study by Wanitphakdeedecha [24] on 25 nails of 14 patients using long-pulsed Nd:YAG 1,064 nm for four sessions at a 1-week interval. They reported a mycological response rate of 48% 1 month after treatment.

This is due to the fact that the amount of laser energy that can deactivate 80–90% of the organisms present in an affected nail does not instantly kill the fungal colonies but limits their ability to replicate or survive [25].

Group II showed mycological clearance in 30% only. However, after 6 months follow-up, it became statistically significant with 50% mycological cure. Similar results were reported by Kalokasidis et al. [26] that showed statistically significant mycological cure after 3 months follow-up but with a higher percentage (95.42%).

Another study by Galvan Garcia [27] revealed 100% mycological cure after a 9-month follow-up.

The present study revealed a clinical success of 70% in group I that was increased to 80% by the end of the follow-up period.

Similar findings were reported by Kim et al. [28] using Nd:YAG laser show clinical improvements at 12 and 24 weeks, presented 47.6% and 57.1% in group A using a 0.3 milliseconds pulse duration, 5 mm spot size, 16 J/cm2 fluence and 10 Hz and show clinical improvements of 26.3% and 36.8% in group B using 0.6 milliseconds, 2 mm, 225 J/cm2 and 5 Hz [28].

Also the study of Leverone et al. [29] using Nd:YAG revealed clinical improvement in (40.6%) of patients and failure in (59.4%) at the end of the treatment sessions. while at the end of 18-month follow-up period; (35.3%) of patients, continued to show improvement, and (64.7%) had treatment failure.

Group II showed clinical success in 90% at the end of the session and the same was found at a 6-month

follow-up. These results are similar to the results of Galvan Garcia [27] using Q-Switched showing a clinical improvement of 93% at the end of the session and 100% after a 6-month follow-up.

According to proximal nail measurement, there was a statistically significant improvement in both groups with no statistically significant difference between them at the end of the sessions and after a 6-month follow-up. Similarly, Kostas Kalokasidis et al. [26] and Ortiz et al. [30] using Q-Switched and long-pulsed laser respectively, showed significant improvement in proximal nail measurement.

The present study was in contrast to the study of Hollmig et al. [31] using long-pulsed Nd:YAG, only two sessions, that showed a statistically insignificant difference between the treated and control group in proximal nail measurement and also in mycological clearance after treatment and after 1-year follow-up.

The present study revealed an insignificant relationship between mycological response at end of the session and both types of fungus and clinical type of onychomy-cosis in both groups. However, another study by KostasKalokasidis et al. [26] showed a significant relationship between them and mycological response at end of treat-ment as it showed that the clinical type of onychomycosis seems to have an important influence on response: “distalsubungual” had the best response followed by “lateraledge, dystrophic type, and superficial white”; however, “proximal subungual” type showed the lowest response. Dermatophytes (T. rubrum) seem to have the best response rate followed by T. mentagrophytes and Candida came last. This difference may be due to the difference insample size, and also the present study did not have allclinical types of onychomycosis [26].

A mild to moderate pain sensation was the mostcommon side effect of treatment in both groups, it wasrelatively higher in group I but not to a statistically sig-nificant level. Nail discoloration, slow growth, and acuteparonychia were also reported by some patients, but werenot statistically significant.

The side effects reported by Kozarev et al. [25] were46% mild pain and 28% moderate pain that decreasedevery session, and also discoloration of affected nails.

CONCLUSIONS

(1) Owing to clinical and mycological cures, both long-pulsed Nd:YAG (1064 nm) and Q-Switched Nd:YAG (1064 nm) laser can be used as a safe and effective modality in treatment of onychomycosis, particu larly in patients who refuse or have contraindication to oral antifungal treatment.

(2) There is no statistically significant difference between both types of laser in treatment of onychomycosis but the Q-Switched laser sessions were less frequent than Nd:YAG and also it had fewer side effects, as regards severity of pain sensation during the procedure than long-pulsed Nd:YAG.

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