LETTER TO THE EDITOR

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Safety and Cinical Outcomes of the 1064 nm Neodymium-doped Yttrium Aluminum Garnet (Nd:YAG) Laser Combined with Topical Antifungal Agents for Onychomycosis in Patients with Diabetes Mellitus

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Onychomycosis is the fungal infection of the nail bed, matrix, and plate. Prevalence of onychomycosis is 2 to 13% of the general population, and higher in the elderly, reaching 14 to 28%[1]. Diabetes mellitus (DM) is with an estimated 60 million people worldwide. Complications of DM affect all systems of the body, of which decreased perfusion of the lower extremity may be compounded by infections such as onychomycosis and bacterial sepsis, and peripheral neuropathy[2]. Prevalence of onychomycosis in DM patients is high, approximately one third of patients with diabetes[2]. Furthermore, the risk of developing complications from onychomycosis increases, and the treatment failure risk of oral antifungal agents in diabetic patients is high due to poor patient compliance, drug interactions and decreased immune status[3].

Neodymium-doped yttrium aluminum garnet (Nd:YAG) laser is the first laser device designed specifically for the treatment of onychomycosis, and approved by the Food and Drug Administration for the temporary increase of clear nail in patients with onychomycosis. It has recently been widely used as one of therapeutic options for onychomycosis[4]. However, there are only a few reports on the safety and clinical outcomes of Nd:YAG laser treatment for onychomycosis in patients with DM. The purpose of this study is to evaluate safety and the outcomes of 1064 nm Nd:YAG laser treatment for onychomycosis with DM.

A retrospective chart review of patients who visited the department of dermatology at Kyung Hee Medical Center (KHMC) and Arumdaun Nara Dermatologic Clinic, from January 1, 2013 to July 30, 2019 was performed. The Ethics Committee of KHMC (Institutional Review Board approval #KHMC IRB 2019-11-078) approved the study. Patients with diabetic foot ulcer and sensory loss were excluded for the safety problem. Diagnosis of onychomycosis is based on microscopic examination after treatment with 20% KOH and fungal culture using Sabouraud's dextrose agar. Only patients with type 2 DM which was diagnosed by endocrinology physicians were included in this study. Nails with onychomycosis were treated by topical antifungal agent (Loceryl nail lacquer, Exoderil, and Jublia) and 1064 nm Nd:YAG laser (Pinpointe™ Footlaser™; Pinpointe USA Inc.) at the following settings: pulse energy, 200 mJ; pulse width, 0.1 ms; spot size, 1.5 mm; frequency; 30 Hz; 2 passes at each session, total 4 to 6 sessions at 4-week intervals. Despite the clinical protocol[5], in which the irradiation area included total toenail plus a 2~5 mm margin, we did not

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Table 1. Clinical characteristics and response rate of each subgroup

	Controlled DM group	Uncontrolled DM group	Healthy group	*p*-value
Number of patients	20	20	20	
Average age	66.90	63.15	64.40	.586
Sex (male/female)	11/9	7/13	9/11	.459
Number of nails	59	64	69	.447
Average response rate (%)	**31%**	**30%**	**30%**	**.985**

Average response rate = Onychomycosis Severity Index of posttreatment / Onychomycosis Severity Index of pretreatment

Table 2. Response rate of each subtype of onychomycosis.

Nail number (response rate)	Controlled DM group	Uncontrolled DM group	Healthy group	*p*-value
Distal lateral subungual onychomycosis	56 (0.32)	52 (0.32)	62 (0.28)	.693
Proximal subungual onychomycosis	0	0	1 (1)	–
White superficial onychomycosis	0	1 (0.9)	4 (0.37)	–
Total dystrophic onychomycosis	3 (0)	11 (0.15)	2 (0.49)	.356

irradiate the boundaries of toenails and skin with lasers to reduce the risk of burn with diabetic patients and healthy control.

Clinical outcomes were evaluated by the Onychomycosis Severity Index (OSI) score method and performed before the treatment and 4 weeks after final laser therapy[6]. Response rate was defined as the percentage of posttreatment OSI divided by the initial OSI. We classified onychomycosis patients into 3 age- and sex-matched groups; controlled DM patients, uncontrolled DM patients, and heathy control group. Controlled blood glucose level was defined by American Diabetes Association Standards of medical care in diabetes 2017, as heamoglobin A1c (HbA1c) < 7.0%. All statistical analyses were performed using SPSS software (version 20.0; SPSS Inc., Chicago, IL, USA).

A total of 60 patients were included in this study, and each group had 20 patients. Mean age of the patients of each group was 66.9 in the controlled DM group, 63.2 in the uncontrolled DM group, and 64.4 in healthy group. Male-to-female ratio of each group was not significantly different (Table 1). The average response rates (posttreatment OSI/pretreatment OSI) were about 30% in all three groups, which were not significantly different among the three groups (p=0.985). When we divided clinical presentation into subtypes of OM, the most common subtype was distal lateral subungual onychomycosis (DLSO). There was no significant difference in treatment response among DLSO type of the three groups (Table 2). There were no sustained adverse effects, such as edema, burning, blister, infection, nerve damage, and delayed wound healing, after the treatment other than a temporary heating sensation in all groups.

There have been few studies on safety and clinical outcome of 1064 nm Nd:YAG laser treatment in diabetic patients[7]. Our study is a rare study evaluating the outcome of 1064 nm Nd:YAG laser treatment in diabetic patients. In the literature, adverse effects of laser treatment occurred usually only during treatment, which were feeling of mild burning or tingling sensation at the laser irradiated site. Severe adverse effects following laser treatment, such as deformity of nails or infections, have been usually not reported. Karsai et al. showed the profile of severe adverse effects of laser treatment; edema, burning, blisters, infections, nerve damage, and delayed wound healing. However, no adverse effects were observed in the laser group[8]. In our study 1064 nm Nd:YAG laser treatment showed no adverse effects in all groups. Therefore, 1064 nm Nd:YAG laser treatment can be used safely in diabetic patients.

All subjects in three groups were treated with combined topical antifungal agent and laser treatments. By applying a topical agent to the periungual skin and not applying laser in this area, it would be possible to reduce the possibility of

burns caused by laser irradiation and to obtain additional therapeutic effects by combined treatment.

There is little research on the association between blood glucose control and prognosis of onychomycosis. Eckhard et al. showed that the prevalence of positive fungal samples of the foot is significantly higher for participants with less controlled blood glucose (higher HbA1c)[9]. However, in our study, therapeutic response to 1064 nm Nd:YAG laser treatment of onychomycosis in controlled DM patients was not significantly different from that in uncontrolled DM patients. Patients with DM may have comparable complete cure rates as nondiabetics, but duration to complete cure is longer and recurrence rates are higher[10]. Therefore, diabetes control may affect other therapeutic aspects of onychomycosis in addition to the cure rates. Limitations of this study are retrospective chart review and small sample size. Some factors related to poor prognosis were not considered in this study, such as nail infection by non-dermatophyte mold or yeast. In addition, long-term follow-up will be needed to identify the recurrence or new infection of onychomycosis in diabetic patients. In conclusion, The 1064 nm Nd:YAG laser may be a safe alternative treatment option for onychomycosis in diabetic patients.

Key Words: Diabetes mellitus, Nd:YAG laser, Onychomycosis, Safety

ETHICAL APPROVAL

The study was approved by the Institutional Review Board and performed in accordance with the principles of the Declaration of Helsinki.

CONFLICT OF INTEREST

In relation to this article, we declare that there is no conflict of interest.

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