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APPLICATION OF LASER TECHNOLOGIES IN TREATMENT OF ONYCHOMYCOSIS.

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Abstract:

Onychomycosis is a common nail pathology which has proven to be a treatment challenge to healthcare professionals. Antifungal drugs have been the mainstay of therapy for many years. Recently, laser technologies have been introduced as a treatment for onychomycosis avoiding the disadvantages of systemic and topical drug therapies, offering a rapid treatment for an often-persistent nail condition. The purpose of this study was to review published evidence regarding the effectiveness of laser technologies in the treatment of onychomycosis

Keywords: Laser, Nd-YAG laser, CO_2 laser, onychomycosis, single rate, systematic review

Onychomycosis is a chronic fungal infection of the nail that may involve the nail bed, plate or matrix. It is difficult to cure and relapses are common. The condition is caused by dermatophytes, principally *Trichophyton rubrum*, *Trichophyton mentagrophytes* and *Candida albicans*.[1] Clinical classification is performed according to the specific site of infection and includes superficial white onychomycosis, proximal subungual onychomycosis, distal and lateral subungual onychomycosis and total dystrophic onychomycosis. Of these, distal and lateral subungual onychomycosis are the most common.[2] Traditional treatments for onychomycosis comprise topical, oral, mechanical and chemical therapies.[3] Topical drug treatments are not usually successful because they are unable to penetrate the nail plate.[4,5] Oral antifungal agents can produce adverse reactions due to a significant risk of liver and kidney toxicity and drug interactions occurring within the body.[6] Topical antifungal treatments can be more effective when combined with surgical removal or chemical dissolution of the nail plate.[7] In 1984, Apfelberg[8] began using laser treatment for onychomycosis, and since that time laser treatments such as long-pulsed 1064-nm Nd: YAG lasers, short-pulsed 1064-nm Nd: YAG lasers, CO_2 lasers and lasers with wavelengths of 870nm, 930nm and 1320nm have begun to emerge as new therapies for the treatment of onychomycosis.[9] Compared with topical and oral therapies, laser treatment offers a more promising therapy for the treatment of the condition in diabetics, elderly patients with drug intolerance, and those with liver and kidney disease.[10] However, available evidence concerning its efficacy for the treatment of onychomycosis is contradictory.[11] We therefore conducted a meta-analysis of data extracted from available published studies on laser treatment in the context of onychomycosis, in order to evaluate the efficacy and safety of the available different laser devices. It was anticipated that the results would inform and guide future clinical application of laser treatment technologies for onychomycosis.

The study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. We searched electronic databases (PubMed, Web of Science) for studies published up to July 2018 using the Mesh terms "laser, onychomycosis" and "laser, tinea unguium". We also searched electronic Chinese databases (CNKI, WanFang Database and VIP) for studies published up to July 2018 using the Chinese keywords "laser, onychomycosis," and "laser and onychomycosis". The inclusion criteria for the study were as follows:

(1) Randomized Controlled Trial (RCT) or clinical study in which the onychomycosis group received only laser treatment;

(2) onychomycosis diagnosed by mycological examination;

(3) study purpose related to the efficacy of laser treatment for onychomycosis;

(4) patients had not been treated with systematic antifungal drugs during the preceding 6 months and exhibited no abnormal clinical manifestations

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associated with other skin diseases such as psoriasis or lichen planus; (4) the treatment group was treated by laser and the control group comprised either a blank control, self-control, and/or laser treatment combined with other treatment options; and
(5) mycological cure rate and clinical cure rate of diseased nail reported. Since clinical cure rates can vary markedly with different treatments, a meta-analysis of mycological cure rates was performed.

The exclusion criteria were as follows:
(1) case reports;
(2) duplicate publications
(3) conference papers, systematic reviews, and meta-analyses
(4) studies in which the laser treated group also received other forms of treatment.

The systematic search of the literature identified 681 potentially relevant articles. After removing duplicate publications, 104 articles remained and were subjected to preliminary screening of abstracts 1). Following the exclusion of descriptive studies and studies that included other therapies in addition to laser treatment, 35 articles remained that met the eligibility criteria. These 35 articles involved 1723 patients and 4278 diseased nails. The studies included 5 RCTs.

The meta-analysis performed in this study was conducted on data extracted from 35 articles, including 5 RCT studies, 1723 patients and 4278 diseased nails. The included studies did not show evidence of publication bias and the risk of selective reporting was determined as being low. The majority of the included studies were scored as being of medium quality or above. In general, the analysis revealed that the efficacy of laser treatment of onychomycosis was approximately 63%. In comparison, the mycological efficacy of itraconazole pulse therapy and continuous terbinafine therapy for the treatment of onychomycosis were 79.6% and 84.8%, respectively. Thus, the overall efficacy of laser treatment was moderately lower than that of conventional oral drug treatments, but it produced less reported side effects, such as damage to the liver and kidney or gastrointestinal reactions.[17] Further, the data suggested that laser treatment appeared to be more suitable for certain population subgroups, such as children, the elderly and pregnant women.

The efficacy of CO_2 laser-treatment was found to be slightly higher than that of 1064-nm Nd: YAG laser treatment for curing onychomycosis. This may be because whilst the 1064-nm laser inhibits the growth of the fungus, the CO_2 laser can increase the localized temperature and gasify and decompose the infected tissue and have a sterilizing effect. However, differences between the number of included cases within each of these treatment groups may have influenced the result. The long-pulsed 1064-nm Nd:YAG laser exhibited better efficacy than the short-pulsed 1064-nm Nd:YAG laser. Rungsima et al considered the long-pulsed 1064-nm laser to be more easily absorbed by melanocytes, giving rise to better therapeutic results. The cytoderm of *Trichophyton* fungi contains a large amount of melanin, and the absorption spectrum of its chromophore is 1064nm. This means that the long-pulsed 1064-nm Nd:YAG laser can act directly on the chromophore, resulting in a localized increase in temperature and subsequent destruction of the fungi. On the other hand, the short-pulsed 1064-nm Nd:YAG laser acts on the diseased nail, causing tiny bubbles to form and producing sonic shock waves which can significantly inhibit the growth of the fungal colony. Karsai et al reported that short-pulsed 1064-nm Nd:YAG laser treatment had no effect on either the mycological cure rate or on clinical improvement of onychomycosis caused by *T. rubrum*. It may be that the longer follow-up period of the RCT study (12 months) led to a relatively high recurrence rate or that there was a decrease in the number of potential target chromophores which affected (reduced) the laser-tissue interaction.

The present analysis also revealed that the efficacy of CO_2 perforated laser treatment was superior to that of CO_2 fractional laser treatment in curing onychomycosis. Among the analyzed studies, the cure rate produced by CO_2 fractional laser treatment was 45%, while the cure rate of CO_2 perforated laser treatment was 95%. Further, the bacteriostatic and sterilizing effects of CO_2 laser treatment did not appear to produce the types of side effects reported for the conventional oral drug therapies. On this basis, Yang et al considered that the efficacy of fractional CO_2 laser treatment could be improved by extending the duration of treatment. Because of its photothermal effect, perforated CO_2 laser treatment can gasify and entirely decompose the infected tissue, which is likely to achieve a better long-term effect due to improved sterilization. However, compared to CO_2 fractional laser treatment, CO_2 perforated laser treatment produces a higher localized temperature, which can be difficult to control in terms of the depth of laser penetration into the tissue, and which can therefore result in larger wounds, forming a brown eschar and higher risk of bleeding. It is therefore necessary to avoid excessive pursuit of curative effects where the treatment itself may cause excessive clinical damage of the nail bed and deck.

The efficacy of laser treatment in curing onychomycosis depends significantly on the health condition of the patient and on the course of treatment being completed. Carney et al showed that

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grinding of the diseased nail before treatment in order achieve a thickness of less than 2mm was conducive to laser penetration. Where more than 50% of the diseased nail is affected, malnutrition of the nail and/or invasion of the nail matrix have a detrimental effect on the prognosis following laser treatment. In all except five of the included articles, the laser treatment was repeated at least 4 times. It is therefore considered that changing the treatment duration and the total length of the treatment course could improve the mycological cure rate and clinical efficacy of laser treatment of onychomycosis. In addition to the 1064-nm Nd:YAG laser and CO_2 laser, Landsman et al used 870-nm and a 930-nm lasers to treat severe onychomycosis and this produced a mycological cure rate of only 38%. Ortiz et al used a 1320-nm Nd:YAG laser to treat onychomycosis but reported that this produced a lower curative efficacy than the control group. For this reason, 1064-nm Nd:YAG lasers and CO_2 lasers are more commonly used than 1320-nm Nd:YAG lasers. It is worth noting that many studies found that the mycological and clinical efficacy of laser treatment combined with topical drugs was significantly higher than that produced by laser treatment alone, which may be related to the effects of laser treatment in enabling the drugs to penetrate deeper into the nail deck.

Laser treatment (using a 1064-nm Nd: YAG laser or perforated CO_2 laser) for the treatment of onychomycosis has a high mycological cure rate and high safety record, and can be used successfully for the treatment and cure of onychomycosis.

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