Fractional CO\(_2\) Laser in the Management of Onychomycosis

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**Context:** Pharmacotherapy is the standard first-line management of onychomycosis (OM). Prolonged treatment courses have reported cure rates of only 40%–80%. Although lasers have been approved by the US Food and Drug Administration for the clearance of nail in OM, their efficacy in the first-line management is not established. In this context, we conducted a study with the aim to ascertain efficacy of fractional CO\(_2\) laser along with topical 1% terbinafine cream in the management of OM.

**Settings and Design:** This was a single-arm observational study in OM administered treatment over 16 weeks and analyzed at 6 months after the initiation of treatment.

**Subjects and Methods:** Treatment naive and others after a 3 month washout period were administered fractional CO\(_2\) laser using pulse energy of 110 mJ, a density of 256 spots/cm\(^2\), pulse interval of 0.5 mm, pulse duration of 0.1 ms, and a rectangular spot size of 2–10 mm length and 0.6–5 mm breadth, every 4 weeks for four sessions along with 1% topical terbinafine cream. Outcome was assessed with Onychomycosis Severity Index (OSI), Visual Analog Score, mycological cultures and potassium hydroxide (KOH) mount at 16 weeks and 6 months after initiation of treatment.

**Used:** Paired \(t\)-test was used to compare the change in OSI.

**Results:** Mycological evaluation at the end of 16 weeks revealed that 90% (45 nails) were KOH negative and 88% (44 nails) were culture negative. Evaluation at 6 months revealed that 86% (43 nails) were KOH negative and 88% (44 nails) were culture negative. OSI improvement compared to baseline was good to complete in 42 cases, and Visual analog Score revealed 36 nails showing 3+–4+ improvement.

**Conclusions:** Fractional CO\(_2\) laser is a viable alternative to oral antifungals, especially when they are contraindicated such as in military aviators and in cases where drug interactions are suspected.

**Keywords:** Fractional CO\(_2\) laser, onychomycosis, terbinafine

**Introduction**

Onychomycosis (OM) or fungal infection of the nail apparatus involves either toe or fingernails causing pain, discomfort, disfigurement, and discoloration. The resultant nail may produce serious physical, occupational limitations, and affect the quality of life. The prevalence of OM is reported as 0.5%–5% in India\(^1\) and up to 11% across Europe\(^2\) accounting for 50% of all nail diseases.\(^3\) Treatment of OM is time-consuming, cost-intensive, and has cure rates of only 40%–80%. Various treatment modalities available for the treatment of OM include systemic antifungal treatments, surgical nail avulsion, long pulse, and Q switched Nd: YAG laser for nail clearance. Topical antifungals by themselves are not effective. Pharmacotherapy is the standard first-line management of OM. Prolonged treatment courses have reported cure rates of only 40%–80%.\(^4\) Although lasers have been approved by the US Food and Drug Administration for the clearance of nail in OM, their efficacy in the first-line management is not established.\(^5\) In this context, we conducted a study with the aim to ascertain efficacy of fractional CO\(_2\) laser along with topical 1% terbinafine cream in the management of OM.

**Subjects and Methods**

We, at the skin department of a tertiary care hospital, conducted a single-arm observational study on OM between September 1, 2016 and December 31, 2017, on fifty nails to assess the rate of clearance of the nails’ off OM. Fifty onychomycotic nails...
of patients above 18 years of age presenting for treatment were categorized as one of the following standard patterns: distal subungual OM, proximal subungual OM, superficial white or black OM, and mixed dystrophic onychomycosis (TDO). Diagnosis was confirmed by nail clipping-potassium hydroxide (KOH) mount/culture. Molds were only considered pathogenic if these cases demonstrated nail abnormalities consistent with diagnosis, with demonstrated growth on culture of more than five colonies of the same mold in the absence of dermatophyte growth in at least two consecutive nail samplings. Patients who had used systemic or topical antifungals in the preceding 3 months before the first scheduled laser session; other nails disorders such as bacterial infections, subungual hematoma, and associated nail disorders which produce changes in the nail plate; and pregnant women were excluded from the study. Only three nails had history of being treated, two with a 6-month course of itraconazole, and one with fluconazole for 3 months. These three cases had discontinued treatment and had again reported after 4–6 months of discontinuation of earlier treatment. Nail severity was assessed at baseline by measuring the Onychomycosis Severity Index (OSI) for initial assessment and for follow-up along with Visual Analog Scale. Outcome was assessed with OSI as complete: 100%, good: >60%, inadequate: 20%–60%, and poor: <20%. Visual Analog Score assessed outcome as very much improved (>76%): 4, much improved (51%–75%): 3, moderately improved (26%–50%): 2, poorly improved (0%–25%): 1, and no improvement (0%): 0.

All infected nails were initially cleaned with normal saline and allowed to dry, and any cosmetic nail lacquer if present was removed. They were then treated with fractional CO\(_2\) laser using pulse energy of 110 mJ, a density of 256 spots/cm\(^2\), pulse interval of 0.5 mm, pulse duration of 0.1 ms, and a rectangular spot size of 2–10 mm length and 0.6–5 mm breadth. Three passes were administered at the same site in static operating mode over the affected area including 1-mm normal-appearing areas around them every 4 weeks for four sessions (0, 4, 8, and 12 weeks). No local anesthesia was used. All cases were prescribed topical 1% terbinafine cream for application over the affected nails twice daily during the study period. Follow-up was performed at each visit at 4-week intervals (4, 8, 12, and 16 weeks after the initiation) with an assessment of clinical improvement using the OSI score, photography, patient Visual Analog Score, and adverse effects. Mycological cultures and KOH mount were repeated at 16 weeks and 6 months after the initiation of treatment.

End points of the study were defined as at least 3 mm clearance in 16 weeks, severe intractable pain or intolerance to laser, nail fold side effects with fissuring, erythema, scaling and pain, onycholysis, or onychoschizia.

**Results**

Twenty-six patients with fifty affected nails completed the study [Figures 2 and 3]. Seventeen were male and rest nine were female with a mean duration of disease of 3.2 years. The average age group of the study population was 56 years. The most common type of OM included in the study was TDO (34 nails). Of the 26 patients, 16 had diabetes mellitus and were mainly in the TDO group, 11 were hypertensive, 3 had hypothyroid, and 1 had pulmonary tuberculosis.
The most common organism isolated belonged to *Trichophyton* genus in 24 nails [Table 1]. Assessment was done at 16 weeks and 6 months and revealed nail clearance of over 3 mm in 46 nails.

OSI improvement compared to baseline was good to complete in 42 cases [Figure 4]. Visual Analog Score revealed 36 nails showing 3+–4+ improvement.

Mycological evaluation at the end of 16 weeks revealed that 90% (45 nails) were KOH negative and 88% (44 nails) were culture negative. Evaluation at 6 months after initiation revealed that 86% (43 nails) were KOH negative and 88% (44 nails) were culture negative. Culture from six culture-positive nails revealed *Trichophyton* spp. All six had TDO form of OM.

**DISCUSSION**

OM is known to be difficult to treat. Extended doses of oral antifungals needed up to 18 months in some cases. Failure to achieve a cure and relapses due to residual spores are well known.[7,8] Further antifungal drugs are contraindicated in military flying aircrew,[9] in patients with active or chronic liver or renal disease, and are sometimes declined by patients seeking alternatives to oral medication. Topical therapy in the form of lacquers is prolonged, whereas other preparations are unable to penetrate the diseased nail plate.[10] Hence, nonpharmacologic treatment modalities have emerged for rapid and effective treatment for persistent nail infection. These include photodynamic therapy, infradiode lasers, long pulse and Q-switched Nd: YAG lasers, and fractional CO₂ laser. In OM, all lasers exert their effect by “selective photothermolysis,” delivering of a short burst of laser light energy into the target tissue causing a rapid elevation in temperature into the defined target area.[11] Temperatures more than 50°C have been demonstrated to have a direct thermal killing effect on fungal mycelia. Chitin surrounding the fungal mycelium is slow to dissipate heat, resulting in heat buildup and rising temperature results in fungicidal effect.[11] The ablative fractional CO₂ laser is based on the principle of fractional thermolysis which makes the use of microthermal zones of tissue damage to deeper layers which make it useful to enhance the penetration of topical agents. Fractional CO₂ laser provides short recovery times and decreased pain compared with traditional, continuous CO₂ lasers.

Worldwide, OM is mainly caused by dermatophytes, and about 10% are due to nondermatophytes.[12] In India, the most common species are *Trichophyton rubrum* and *Trichophyton interdigitale* which account for about 85%–92% and rest by various other dermatophytes and nondermatophyte molds.[13] Toenail OM is more common in males owing to trauma, prolonged outdoor activities, and wearing occlusive footwear all of which an armed forces personnel is exposed too. Our study too revealed the most common fungi to be *Trichophyton* sp., followed by *Aspergillus* sp. [Table 1]. Toenail involvement was consistent with literature reported.[4]

### Table 1: Fungal culture species on culture and response to treatment

| Species                  | Initial | 4 months | 6 months |
|--------------------------|---------|----------|----------|
| *Trichophyton*           | 24      | 1        | 1        |
| *Aspergillus fumigatus*  | 10      | 3        | 3        |
| *Aspergillus niger*      | 8       | 2        | 2        |
| *Acremonium*             | 4       | 0        | 0        |
| Non Albicans Candida     | 3       | 0        | 0        |
| *Candida albicans*       | 1       | 0        | 0        |

![Figure 3: Pretreatment (top row) and posttreatment (bottom row) at 6 months](image)

![Figure 4: Visual Analogue Score at 16 weeks (above) and onychomycosis score index on follow-up (below)](image)
There have been few studies which have evaluated the efficacy of fractional CO$_2$ laser in the treatment of OM. These studies administered fractional CO$_2$ laser for 3–6 sessions in combination with topical antifungals or photodynamic therapy. In our study, we too used topical terbinafine; however, we followed up the patients for 6 months after completion of treatment. Lim et al. administered fractional CO$_2$ with topical terbinafine and followed up for 3 months with a 50% complete response, whereas Shi et al. in thirty cases with 124 nails found a clinical efficacy rate of 68.5%, 3 months after the last session. Studies have been done using topical luliconazole and topical ticonazole, and photodynamic therapy.

Q-switched Nd: YAG laser as compared to other laser devices delivers higher energy in short pulses, thus causing photomechanical disruption in absence of attendant normal tissue damage, and may also cause vasodilation and immunological stimulation. Gupta and Versteeg analyzed ten trials of lasers in OM from 2010 to 2014, reviewing their different parameters and results. The studies claimed that Nd: YAG can achieve a success rate of 60%–95% in accelerating nail clearance of the fungus over a treatment period of 3–6 months. Karsai et al. in a randomized controlled trial of short-pulsed Q-switched Nd: YAG laser, however, concluded that it was not effective as monotherapy. Two of our cases relapsed at the end of follow-up. Fungal culture in these revealed the same species as initial infection-T. rubrum. A higher clearance at end of treatment hence may not translate to mycological cure in the long term, and these cases need to be followed up till diseased nail clearance is observed. No case experienced side effects limiting their treatment protocol in this study.

Limitations of this study were the sample size of fifty nails, lack of a comparative arm, and an observation period of only 6 months. Confounding effect of past itraconazole and fluconazole treatment in three nails cannot be ruled out conclusively.

**Conclusions**

We conclude that effective nail clearance in OM is possible with fractional CO$_2$ laser. Efficacy of fractional CO$_2$ laser serving as the definitive treatment option in onychomycosis needs corroboration with a larger cohort of patients in studies possibly conducted with a comparative arm of a standard antifungal regimen.

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**Conflicts of interest**

There are no conflicts of interest.

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