

An Observational Study On Efficacy Of Fractional CO₂ Laser Assisted Topical Antifungal Therapy For The Treatment Of Onychomycosis In Adult North Indian Population

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ABSTRACT

Background: Onychomycosis, a fungus that affects the nails, is typically brought on by dermatophytes, as well as nondermatophytes, moulds, and yeasts. Using a fractional CO₂ laser to treat onychomycosis results in microscopic thermal wounds in the nails, which help topical antifungal medications penetrate the nail more effectively.

Aims and Objectives: To study the efficacy of fractional CO₂ laser assisted topical antifungal therapy for onychomycosis treatment in adult north Indian population.

Material & Method: In this study, 50 clinically suspected patients with onychomycosis had their nails examined by KOH examination and culture in both males and females over the age of 18. All patients underwent fractional CO₂ laser treatment every two weeks while also receiving randomly selected topical antifungal drugs for a total of six months. Clinical findings and the Scoring Clinical Index were used to analyse the nails of all the patients for onychomycosis.

Result: All patients with KOH and culture-proven onychomycosis had clinical improvement, as determined by calculating the Scoring Clinical Index for onychomycosis following the conclusion of treatment, since there was a significant drop in the score of SCIO in all patients.

Conclusion: Fractional CO₂ Laser assisted topical antifungal therapy is effective treatment for the onychomycosis in adult north Indian population.

Keywords: Onychomycosis, Antifungal Drugs, CO₂ Laser.

Introduction

Onychomycosis is an infection of the nail unit caused by fungus (dermatophytes, non-dermatophytes, and yeasts), manifesting as nail discolouration, onycholysis, and thickening of the nail plate.

Onychomycosis is categorised as distal lateral subungual onychomycosis (DLSO), superficial onychomycosis, proximal subungual onychomycosis (PSO), endonyx onychomycosis, and

complete dystrophic onychomycosis (TDO).

90% of toenail onychomycosis and 75% of fingernail onychomycosis are caused by dermatophytes, specifically *Trichophyton mentagrophytes* and *Trichophyton rubrum*⁹⁻¹³. *Aspergillus* species, *Scopulariopsis* species, *Fusarium* species, *Acremonium* species, *Syncephalastrum* species, *Scytalidium* species, *Paecilomyces* species.

By coming into direct contact with dermatophytes, non-dermatophyte moulds, or yeasts on the nail, onychomycosis can be contracted. The nail unit is vulnerable to fungal infection because it lacks efficient cell-mediated immunity. The keratin in the nail plate is broken down by fungus-produced enzymes with proteolytic, keratinolytic, and lipolytic activity, which promote fungal invasion of the nail.

Yellow-brown nail discolouration. The nail plate has also been seen to become violaceous, green, or black^[27]. Subungual hyperkeratosis, nail separation from the nail bed (onycholysis), and thickening of the nail plate (onychauxis)^[28] are further clinical signs. Onychomycosis-specific dermatophytoma manifests as linear, single or numerous white, yellow, orange, or brown bands on the nail plate. In comparison to fingernails, toenails are typically impacted seven to 10 times more frequently. The biggest toenails are typically impacted. Typically, tinea pedis is present and multiple toe nails are afflicted.

Treating onychomycosis is problematic for a variety of reasons. Oral therapy is more effective than topical therapy, but it is expensive, requires monitoring for toxicity, and can result in multiple drug interactions. Topical therapy is a long process that often requires nail debridement and multiple return visits and still delivers a relatively poor success rate. The very nature of the hard, protective nail plate itself makes it difficult for topical drugs to reach the fungal pathogens beneath it^[29]. Surgical nail avulsion for the treatment of onychomycosis should be avoided as potential side effects include postoperative pain, narrowing of the nail bed, distal paronychia and infection.

Lasers are viable treatment options for onychomycosis due to their limited contraindications, minimal adverse effects, short treatment regimens, and high patient compliance. CO₂ laser therapy is the oldest form of laser treatment for onychomycosis. As an ablative laser, it can be used as a primary treatment for onychomycosis or as a supplement to topical antifungals, allowing for penetration through the nail plate to the nail bed.

Laser-heated tissue can cause direct injury or stimulate an immune response against pathogens^[34, 36]. In addition, they have been explored as adjuvants to topical therapy for onychomycosis, as their increased permeability facilitates drug administration through the nail plate^[37]. In conjunction with a topical antifungal agent, relative standard CO₂ proved effective^[38, 39]. However, patients suffered prolonged discomfort following treatment⁴⁰. Yang *et al.*^[41] treated onychomycosis patients with the ablative fractional CO₂ laser for 12 weeks and 8 sessions. 52% of the data demonstrated clinical effectiveness. In two more studies, fractional CO₂ laser was combined with a topical drug (amorolfine and terbinafine, respectively) to treat onychomycosis. Clinical effectiveness was 71% and 73%, respectively.^[42, 43] These findings suggested that a combination of ablative fractional CO₂ laser therapy and topical antifungals may be more successful than fractional CO₂ laser therapy alone. In India, there has been no randomised trial comparing this therapeutic strategy to normal systemic antifungal therapy.

In this study, fractional CO₂ laser-assisted topical antifungal therapy was utilised to treat onychomycosis, and its clinical efficacy was evaluated using the Scoring Clinical Index for Onychomycosis.

Material and Methods

Study design: Hospital based observative study

Study place: Department of Dermatology, Venereology and Leprology, Muzaffarnagar medical college.

Sample size: 50 cases (based on average of past 3 years)

Sampling technique: Simple Random Sampling

Inclusion criteria

Patients of both the sexes, aged between 18 years and 60 years, onychomycosis of toe and fingers of all types diagnosed with clinical nail morphology confirmed by positive fungal microscopy and culture growth, minimum 1 nail involvement and maximum 5 nails including fingernail or toenail or both and patients with negative fungal culture are not excluded if fungal microscopy is positive are included in this study.

Exclusion criteria

Patients below 18 years and above 60 years of age, with history of localized bacterial infections, with concomitant nail disease such as Psoriasis, lichen planus, hematomas or any other skin and nail disease that may interfere with diagnosis, extensive infection of Tinea corporis, Tinea cruris and Tinea manum, Patients having all fingernails or toenail involvement. Patient having allergy to drugs used in treatment in study, Patient with any Cardiac, hepatic, renal disorders, diabetes, HIV and mental illness, Patient who had taken any oral antifungal medication with in last 3 months and Patients with diabetes or any peripheral neuropathy as these patients may not provide feedback about temperature is too high during laser treatment to avoid burning and further complications ^[63] are excluded from this study.

Materials required

Digital Camera, 15 number sterile scalpel, 20 Percent KOH solution, Microscope, Glass slides and cover slips, Culture media of Sabouraud's dextrose agar with chloramphenicol and cycloheximide, Antifungal sensitivity kit, Fractional Carbon dioxide laser machine and Topical antifungal drugs.

Procedure

A detailed history of every patient along with the complaints, duration of illness was taken. The physical features of affected nails along with those of nail folds were noted. The presence of any associated superficial skin infections were looked. All the patients were examined for any other associated skin or systemic disease.

Suspected nails were cleaned with a spirit swab and nails were carefully scraped with a 15 number sterile scalpel blade. In cases where both finger and toe nails were involved, the samples would be taken from both sides. Nail sample was treated with 20 percent KOH solution and slightly warmed, avoiding boiling and nail sample was examined under microscope for fungal and elements and samples were inoculated in culture media of Sabouraud's dextrose agar with chlorophenicol and cyclohexamide. (Hi Media Laboratories) incubated at 37 degree Celsius and examined for every day for 4 weeks.

All the patients were treated with Fractional CO₂ laser (Sellas CIS F1 Laser machine), combined with antifungal drugs at the energy of 10 to 15 mJ, pulse duration of 0.5 to 1 seconds and density of 10 percent over the affected area and spot size of 4 to 8mm. Total 12 sessions of CO₂ laser therapy was done on each patient. Selection of topical antifungal drugs for treatment of onychomycosis was done randomly which mainly include topical antifungal drugs such as Ketoconazole, Terbinafine, Fluconazole, Ciclopirox olamine.

Treatment response in all the patients was analyzed by observing clinical findings and Scoring Clinical Index for onychomycosis before and after the treatment.

The Scoring Clinical Index for onychomycosis was calculated as –

Table 1: Shows various components used and grading of Scoring Clinical Index for Onychomycosis.

| Key Factor | Grade 1 | Grade 2 | Grade 3 |
|------------------------------|--|---------------------------|----------------------------------|
| Clinical form (f) | Distil and lateral subungual onychomycosis | Superficial onychomycosis | Proximal subungual onychomycosis |
| Depth of involvement (d) | <1/3 | 1/3 to 2/3 | >2/3 |
| Degree of hyperkeratosis (h) | Absent or < 1mm | 1-2mm | >2 mm |

Then these values were substituted into the equation ^[69]:

$$\text{Clinical Index Component} = [(d/3)^{3-f} (f + h(3-f))]^{1 - [(2-f)(3-f)/2]}$$

The measurement of nail parameters, nail height, thickness and of nail plate was measured by using a pair of nail calipers.

Using this formula the scoring clinical index for onychomycosis for superficial white onychomycosis, Proximal subungual onychomycosis and Distil subungual onychomycosis the values were calculated and compared before and after the treatment and evaluation of treatment response in all the patients was done through photography, comparing the clinical findings of nails and by calculating the scoring clinical index for onychomycosis after fractional CO₂ laser session every 2 weekly and after 3 months of last treatment.

Patients were consulted well that more than one session or about how many sessions of fractional CO₂ laser were required and informed about total duration of treatment and how much time was needed to see clear nail growth ^[67]. No wound care or dressings were necessary after treatment. Patients was encouraged to keep feet dry and to rotate shoes and socks in case toenail involvement. Patients were made aware of temporary darkening under nail that may occur after laser treatment. Mild analgesics might be used in patients that are complaining of pain after laser treatment and patients were evaluated for other complications after laser treatment such as nail dystrophy and onycholysis ^[70].

Results

The present study observed the efficacy of fractional CO₂ laser assisted topical antifungal drugs therapy. In this study total 50 patients were included and all patients received fractional CO₂ laser assisted topical antifungal drugs therapy for onychomycosis.

Table 2: Shows Types of Onychomycosis seen among patients

| Types of Onychomycosis | Number of cases | |
|--|-----------------|----|
| | N | % |
| Distil Lateral Subungual onychomycosis | 30 | 60 |
| Proximal subungual onychomycosis | 15 | 30 |
| Superficial white onychomycosis | 5 | 10 |
| Total Dystrophic Onychomycosis | 0 | 0 |
| Endonyx Onychomycosis | 0 | 0 |

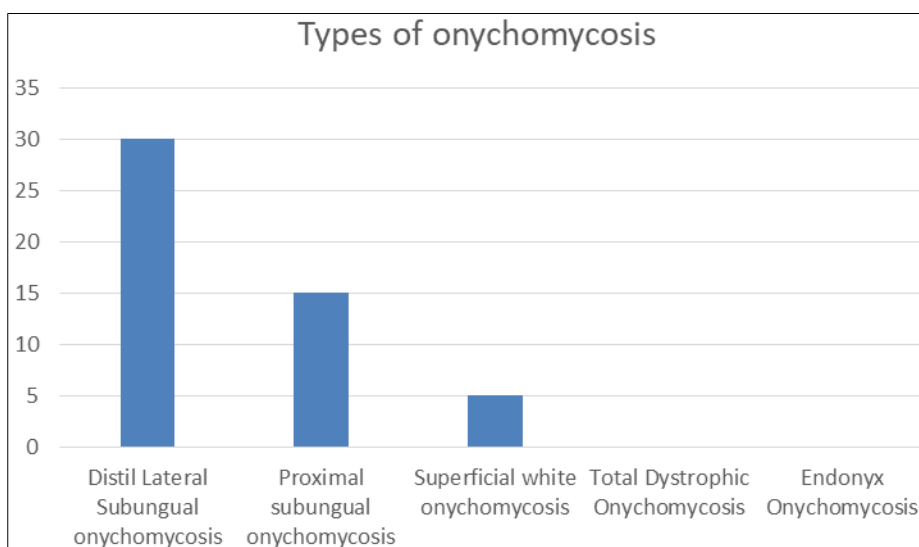


Fig 1: Shows Types of Onychomycosis seen among patients

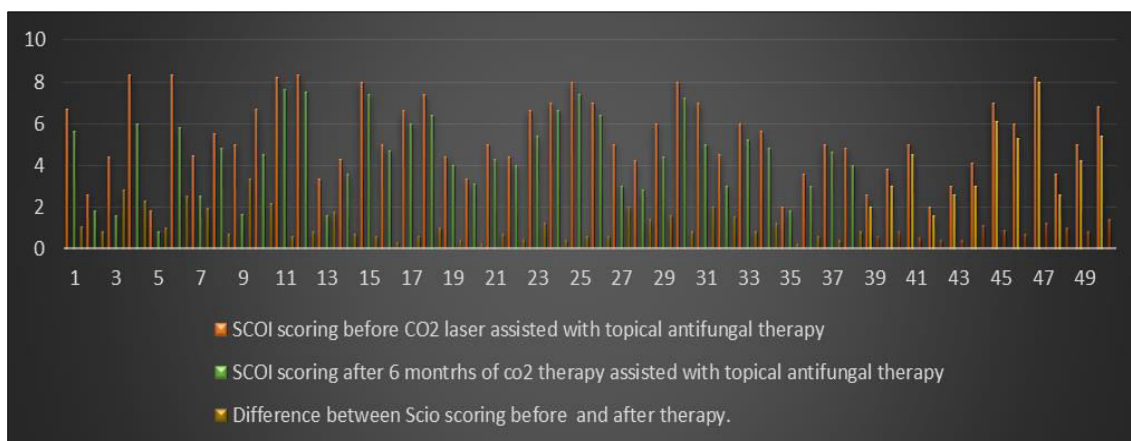
Table 2 and graph 1 shows that majority type of onychomycosis found is Distil Lateral Subungual Onychomycosis which was followed by Proximal Subungual onchnycomycosis and Superfical white onychomycois.

Table 3: Shows the reading of SCIO scoring before starting the therapy and after completion of 6 months of fractional CO₂ laser assisted with topical antifungal drugs therapy

| SCOI scoring before CO ₂ laser assisted with topical antifungal therapy | SCOI scoring after 6 months of CO ₂ therapy assisted with topical antifungal therapy | Difference between Scio scoring before and after therapy. |
|--|---|---|
| 6.66 | 5.6 | 1.06 |
| 2.6 | 1.8 | 0.8 |
| 4.4 | 1.6 | 2.8 |
| 8.3 | 6 | 2.3 |
| 1.8 | 0.8 | 1 |
| 8.33 | 5.8 | 2.53 |
| 4.44 | 2.5 | 1.9 |
| 5.5 | 4.8 | 0.7 |
| 5 | 1.66 | 3.34 |
| 6.66 | 4.5 | 2.16 |
| 8.2 | 7.6 | 0.6 |
| 8.33 | 7.5 | 0.83 |
| 3.33 | 1.6 | 1.73 |
| 4.3 | 3.6 | 0.7 |
| 8 | 7.4 | 0.6 |
| 5 | 4.7 | 0.3 |
| 6.6 | 6 | 0.6 |
| 7.4 | 6.4 | 1 |
| 4.4 | 4 | 0.4 |
| 3.33 | 3.1 | 0.23 |
| 5 | 4.3 | 0.7 |
| 4.4 | 4 | 0.4 |
| 6.6 | 5.4 | 1.2 |
| 7 | 6.6 | 0.4 |
| 8 | 7.4 | 0.6 |
| 7 | 6.4 | 0.6 |
| 5 | 3 | 2 |
| 4.2 | 2.8 | 1.4 |

| | | |
|-----|-----|-----|
| 6 | 4.4 | 1.6 |
| 8 | 7.2 | 0.8 |
| 7 | 5 | 2 |
| 4.5 | 3 | 1.5 |
| 6 | 5.2 | 0.8 |
| 5.6 | 4.8 | 1.2 |
| 2 | 1.8 | 0.2 |
| 3.6 | 3 | 0.6 |
| 5 | 4.6 | 0.4 |
| 4.8 | 4 | 0.8 |
| 2.6 | 2 | 0.6 |
| 3.8 | 3 | 0.8 |
| 5 | 4.5 | 0.5 |
| 2 | 1.6 | 0.4 |
| 3 | 2.6 | 0.4 |
| 4.1 | 3 | 1.1 |
| 7 | 6.1 | 0.9 |
| 6 | 5.3 | 0.7 |
| 8.2 | 8 | 1.2 |
| 3.6 | 2.6 | 1 |
| 5 | 4.2 | 0.8 |
| 6.8 | 5.4 | 1.4 |

It also shows the difference between the SCIO scoring before and after the therapy in patients.



Graph 2: Shows SCIO scoring before CO₂ laser assisted topical antifungal therapy and 6 months of therapy and difference of SCIO scoring before and after therapy.

Table 4: SCIO score before and after therapy among patients

| Interval | Variables | |
|--------------------|-----------|------|
| | Mean | SD |
| Baseline | 5.38 | 1.89 |
| After Intervention | 4.36 | 1.86 |
| Paired t test | 11.30 | |
| p value | <0.01* | |

*: Statistically significant

Table 4, graph 2 shows the comparison of SCIO scoring before starting the therapy and after completion of 6 months of fractional CO₂ laser assisted topical antifungal drugs therapy. Mean SCIO score at baseline was 5.38±1.89 which after intervention reduced to 4.36±1.86 with statistically significant difference when compared using paired t test.

Images



Image 1

Image 2

Image 3

Images 1,2 and 3 shows onychomycosis of index finger of right hand before starting fractional CO₂ laser assisted with topical antifungal therapy, after completion of 6 months of therapy and after 9 months of treatment completion of treatment respectively,



Image 4

Image 5

Image 6

Images 4, 5 and 6 shows onychomycosis of index finger of right hand before starting fractional CO₂ laser assisted with topical antifungal therapy, after completion of 6 months of therapy and after 9 months of completion of therapy respectively.

Discussion

Onychomycosis is a fungal infection of the nail that is growing resistant to many present treatments, necessitating the development of new treatment methods. Current oral and topical antifungal medications (given alone or in combination) are regarded the cornerstone of therapy for onychomycosis. Laser therapies for onychomycosis are the most rapidly developing treatment modality. Laser devices can be utilised to improve drug distribution, activate topically applied pharmaceuticals, and photothermally eliminate fungus. As laser treatments are often administered in the clinic by qualified medical experts, patient compliance is not required. Additionally, they may minimise adverse effects and systemic interactions.

CO₂ laser therapy is an ablative laser, it can be used as a primary treatment for onychomycosis or as an adjuvant to topical antifungals, allowing for penetration through the nail plate and into the nail bed (Lim *et al.*, 2014) ^[43, 68]. There is limited literature on the effectiveness of CO₂ laser systems, particularly among the Indian population.

The aim of the study was to observe the efficacy of fractional CO₂ laser combined with topical antifungal drugs in onychomycosis. In this study total 50 patients were included and treated with fractional CO₂ laser assisted topical antifungal drugs therapy.

Maximum site of involvement was hand as compared to the feet in our study, which might be because hands (fingernails) are more prone to trauma. Additionally, fingernail infections might endanger the patient's life, and nail deformity can lower their self-esteem, forcing them to visit a doctor as soon as possible. Similarly Amr Mohamed Zaki *et al.* ^[68] in their study found that

fingernails were more affected than toenails. This result is consistent with other studies that have demonstrated that fingernail onychomycosis is more prevalent than toenail onychomycosis (Kaur, Kashy *et al.* 2009) ^[68, 71].

Other research, however, indicate that toenail onychomycosis is more prevalent than fingernail onychomycosis ^[72]. In our study, the low frequency of toenail onychomycosis can be linked to the usage of open-toed shoes and a lack of concern about the appearance of the feet and toenails ^[68].

In this study, Distal Lateral Subungual Onychomycosis was the most prevalent kind of onychomycosis, followed by Proximal Subungual onychomycosis.

In their study, Tro V. Chau *et al.* ^[31] discovered that distal and lateral subungual onychomycosis was the most common type of onychomycosis, followed by complete dystrophic onychomycosis and Amr Mohamed Zaki *et al.* ^[68] found that yeast (31%) was the most prevalent fungal species causing onychomycosis in all examined groups, followed by NDM (28.5%), dermatophytes (22%) and trichosporon species infection (18.5%) of cases. Similar findings were observed in a study conducted in Egypt by Abd El-Aal, Abdo, *et al.* (2019) ^[66], who determined that the most frequently identified fungus were yeast infections (37%), followed by NDM infections (22.5%), trichosporon infections (18%), and dermatophyte infections (10%). Overall, the prevalence of causal agents varies by ethnicity and several environmental parameters, such as climate, humidity, occupation, and lifestyle, as well as by geographic location and temporal distribution ^[68].

After fractional CO₂ laser assisted topical antifungal medication therapy, the mean SCOI score decreased from 5.381.89 at baseline to 4.361.89 with a statistically significant difference when compared using the paired t test. Consequently, this mean reduction in SCOI score demonstrated both clinical improvement and the efficacy of fractional CO₂ laser-assisted topical antifungal medications in the treatment of onychomycosis.

It is widely considered that the fractional CO₂ laser treats onychomycosis primarily by its photothermal effect, which raises the temperature of local tissue, thereby killing the fungi in the laser-treated damaged nail. In addition, fractional CO₂ laser causes the local tissue of the afflicted nail to vaporise and exfoliate, resulting in diffuse remodeling, while simultaneously destroying the fungal growth environment, so contributing to the suppression of fungal growth. Additionally, fractional CO₂ laser can boost the absorption of topical antifungal drugs through the densely keratinized, densely calcified nail plate, hence enhancing their penetrance and efficacy. These facts may explain the mycological eradication outcomes of the combined therapy in the present investigation ^[6]. Similar results were observed by Zhou *et al.* (2016) ^[63], who claimed that fractional CO₂ laser combination with 1% luliconazole cream was more successful than fractional CO₂ laser treatment alone 68 in treating infected nails. Zhang *et al.* (2016) demonstrated that the combined therapy with the fractional 2,940 nm Er: YAG laser and amorolfine was significantly more effective than amorolfine alone. In a research by Zaki Am *et al.* ^[68], 120 onychomycosis patients were randomly assigned to one of three groups. Group A patients received fractional CO₂ laser followed by topical tioconazole 28% for five sessions separated by three weeks. Group B participants received fractional CO₂ laser treatment for five sessions separated by three weeks. Patients in Group C received only topical tioconazole 28% for 16 weeks. Analyses were conducted on the clinical effect, KOH examination, and culture of afflicted nails in the three groups. One month following the last session, 55% of Group A patients demonstrated complete clinical improvement, compared to 30% in Group B and 25% in Group C, with a significant difference between the groups.

Naomi Nakano *et al.* (2006) investigated the efficacy of topical antifungal 1% cream in the treatment of onychomycosis. They reported a complete recovery in 77.3% of patients, a significant improvement in 7.6% of patients, and a minor recovery in 1.5% of patients ^[73].

Lecha *et al.* (2002) observed a 69% cure rate with 1% ketoconazole cream once per week for 24 weeks ^[74].

Further prospective studies on larger population of onychomycosis patients and with longer periods of follow-up are recommended. Comparing the effectiveness of fractional CO₂ laser

with other types of lasers in the treatment of onychomycosis and testing the effectiveness of fractional CO₂ laser in combination with other more potent topical antifungals is also recommended. In addition, further research is needed to evaluate the ideal parameters of laser sessions, the number of sessions needed, and the adequate interval between sessions.

Conclusion

Fractional CO₂ laser combined with topical antifungal is a safe and effective treatment for onychomycosis. Fractional CO₂ laser is expected to be an excellent choice for patients in whom systemic antifungals are contraindicated.

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