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Original Research Article

Comparative Study of Fractional CO_2 Laser with Topical 1% Terbinafine Cream versus Oral Itraconazole in the Management of Onychomycosis

Puranik S.[1], Kumar R.[2], Herakal K.C.[3]

[1]Senior Resident, Department of Dermatology, Navodaya medical College, Hospital and Research centre, Raichur, Karnataka, India

[2]Junior Resident, Department of Dermatology, Navodaya Medical College, Hospital and Research centre, Raichur, Karnataka, India

[3]Professor & Head, Department of Dermatology, Navodaya Medical College, Hospital and Research centre, Raichur, Karnataka, India

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Corresponding author: Dr. Shruti Puranik

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Abstract

Background: Onychomycosis is a common fungal infection of the nail unit caused by dermatophytes, yeasts and non-dermatophyte moulds. Oral itraconazole is an effective systemic antifungal agent, but adverse effects, drug interactions and contraindications may limit its use. Fractional carbon dioxide laser combined with topical antifungal therapy has emerged as a useful alternative because it can produce photothermal fungal damage and improve topical drug penetration through the nail plate.

Materials and Methods: This hospital-based comparative interventional study included 40 adults with clinically diagnosed and microbiologically confirmed onychomycosis. Patients were allocated into two equal groups of 20 each. Group A received fractional CO_2 laser therapy along with topical 1% terbinafine cream twice daily, while Group B received oral itraconazole 200 mg twice daily for one week per month for three months. Disease severity was assessed using the Onychomycosis Severity Index (OSI) at baseline and at six months.

Results: The mean age of the study population was 43.84 ± 13.39 years. A total of 93 affected nails were analysed, including 39 nails in the fractional CO_2 laser group and 54 nails in the itraconazole group. Toenail involvement was the commonest pattern in both groups. Distal lateral subungual onychomycosis was the most frequent clinical type, accounting for 76.3% of affected nails. The mean baseline OSI was comparable between Group A and Group B (17.05 ± 9.64 versus 16.90 ± 9.56; p=0.941). At six months, the mean OSI reduced to 8.32 ± 9.70 in Group A and 9.52 ± 9.73 in Group B. The mean reduction in OSI was greater in the fractional CO_2 laser group than in the itraconazole group (8.73 ± 7.04 versus 7.38 ± 6.61), but the difference was not statistically significant (p=0.345). No serious adverse event was observed in either group.

Conclusion: Fractional CO_2 laser combined with topical 1% terbinafine cream and oral itraconazole pulse therapy were both effective in reducing onychomycosis severity. Although the fractional CO_2 laser group showed a slightly greater OSI reduction and better tolerability, the intergroup difference was not statistically significant. Fractional CO_2 laser with topical terbinafine may be considered a promising treatment option, especially for patients in whom systemic antifungal therapy is contraindicated or poorly tolerated.

Keywords: Onychomycosis; Fractional carbon dioxide laser; Terbinafine; Itraconazole; Onychomycosis Severity Index; Dermatophytes.

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Introduction

Onychomycosis is a chronic fungal infection of the nail unit involving the nail plate, nail bed and/or matrix. It is caused mainly by dermatophytes, although yeasts and non-dermatophyte moulds may also be implicated.

The disease produces nail discoloration, subungual hyperkeratosis, thickening, brittleness, onycholysis and cosmetic disfigurement. In India, the reported incidence ranges from 0.5% to 5%, and the disease is often associated with chronicity, recurrence and impaired quality of life. [1,2] Systemic antifungal therapy remains an important treatment modality for onychomycosis.

Itraconazole, a triazole antifungal agent, has a broad spectrum of activity and is commonly used as intermittent pulse therapy. Pulse therapy

provides higher nail drug concentrations with a lower cumulative dose and good clinical response when compared with continuous regimens. [3,4] However, systemic therapy may be associated with headache, nausea, gastrointestinal upset, liver enzyme abnormalities and important drug interactions. Itraconazole is also contraindicated in patients with congestive cardiac failure. [5]

Laser-based treatment is a newer modality for onychomycosis. Fractional carbon dioxide laser acts through selective photothermolysis, producing a photothermal effect on fungal elements; chitin within the fungal cell wall may augment the heating effect. In addition, fractional ablation creates microchannels in the nail plate, thereby facilitating penetration of topical antifungal agents. Recent studies have evaluated fractional carbon dioxide laser in combination with topical antifungal treatment and have reported encouraging clinical and mycological outcomes. [6]

The present study was conducted to compare the efficacy and safety of fractional CO_2 laser combined with topical 1% terbinafine cream versus oral itraconazole pulse therapy in the management of onychomycosis, using the Onychomycosis Severity Index as the primary clinical assessment tool. [7]

Materials and Methods

This hospital-based comparative interventional study was conducted in the Department of Dermatology after obtaining approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants before enrolment. A feasibility-based sample size of 40 patients was selected, with 20 patients in each treatment group. Patients were randomly allocated into Group A and Group B.

Inclusion Criteria: Adults above 18 years of age of either gender, presenting with one or more toenails and/or fingernails clinically suggestive of onychomycosis, were included. Only cases with positive potassium hydroxide mount and fungal culture evidence of fungal infection were considered eligible.

Exclusion Criteria: Pregnant and lactating women, patients with negative KOH mount or negative fungal culture, patients who had used systemic or topical antifungal therapy during the preceding three months and patients with other nail disorders were excluded. Group A received fractional CO_2 laser therapy combined with topical 1% terbinafine cream. A topical anaesthetic cream was applied under occlusion for 45 minutes before laser therapy. All infected nails were treated using fractional carbon dioxide laser with pulse energy of 110 mJ, energy density of 256 spots/cm2, pulse interval of 0.5 mm, pulse duration of 0.1 milliseconds and rectangular spot size of 2-10 mm length and 0.6-5 mm breadth. Three passes were given in static operating mode over the affected area, including 1 mm of surrounding normal-appearing nail. Four laser sessions were performed at four-week intervals. Patients were advised to apply 1% terbinafine cream twice daily throughout the treatment period.

Group B received oral itraconazole 200 mg twice daily for one week per month for three months. Follow-up visits were scheduled at four-week intervals. At each visit, clinical improvement, compliance and adverse effects were recorded. Standardized clinical photographs were taken where feasible. Final analysis was performed at six months after initiation of therapy.

The Onychomycosis Severity Index (OSI) was used to quantify disease severity. The final OSI score was calculated as: score for area of involvement multiplied by score for proximity of disease to matrix, with an additional 10 points added in the presence of dermatophytoma or subungual hyperkeratosis greater than 2 mm. The primary outcome was mean reduction in OSI from baseline to six months. Secondary outcomes included pattern of nail involvement, clinical type of onychomycosis, adverse effects, treatment completion and patient satisfaction. Data were entered into Microsoft Excel and analysed using standard statistical methods. Continuous variables were expressed as mean ± standard deviation, while categorical variables were expressed as frequency and percentage. Intergroup comparison of continuous variables was performed using independent samples t-test or Mann-Whitney U test as appropriate. Categorical variables were compared using chi-square test or Fisher exact test. A p-value less than 0.05 was considered statistically significant.

Results

A total of 40 patients with onychomycosis were included, with 20 patients each in the fractional CO_2 laser with topical terbinafine group and the oral itraconazole group. The mean age of the study population was 43.84 ± 13.39 years. The two groups were comparable with respect to age and gender distribution. The largest proportion of patients belonged to the 51-60 year age group, accounting for 27.5% of the total study population. Overall, 21 patients (52.5%) were female and 19 patients (47.5%) were male (Table 1).

Table 1: Baseline age and gender distribution of the study population

Variable	Fractional laser + terbinafine (n=20)	Itraconazole (n=20)	Total (n=40)	p-value
Age group				0.678
<30 years	3 (15.0%)	6 (30.0%)	9 (22.5%)	
31-40 years	4 (20.0%)	3 (15.0%)	7 (17.5%)	
41-50 years	5 (25.0%)	4 (20.0%)	9 (22.5%)	
51-60 years	5 (25.0%)	6 (30.0%)	11 (27.5%)	
>60 years	3 (15.0%)	1 (5.0%)	4 (10.0%)	
Mean age, years	45.85 ± 13.18	41.83 ± 13.63	43.84 ± 13.39	0.349
Female	9 (45.0%)	12 (60.0%)	21 (52.5%)	0.342
Male	11 (55.0%)	8 (40.0%)	19 (47.5%)	

A total of 93 affected nails were analysed. The fractional CO_2 laser group included 39 affected nails among 20 patients, while the itraconazole group included 54 affected nails among 20 patients.

Toenail involvement was predominant in both groups and accounted for 77.4% of all affected nails. Fingernail involvement was observed in 22.6% of nails.

Distal lateral subungual onychomycosis was the commonest clinical type, followed by total dystrophic onychomycosis and white superficial onychomycosis (Table 2).

Table 2: Distribution according to nail type and clinical type of onychomycosis

Variable	Fractional CO_2 laser + terbinafine (n=39 nails)	Itraconazole (n=54 nails)	Total (n=93 nails)	p-value
Nail type				0.683
Toenail	31 (79.5%)	41 (75.9%)	72 (77.4%)	
Fingernail	8 (20.5%)	13 (24.1%)	21 (22.6%)	
Clinical type				0.274
Distal lateral subungual onychomycosis	27 (69.2%)	44 (81.5%)	71 (76.3%)	
Total dystrophic onychomycosis	10 (25.6%)	6 (11.1%)	16 (17.2%)	
White superficial onychomycosis	2 (5.1%)	4 (7.4%)	6 (6.5%)	

The baseline OSI scores were comparable between both treatment groups for all nails, toenails and fingernails.

In the all-nail analysis, mean OSI decreased from 17.05 ± 9.64 to 8.32 ± 9.70 in the fractional CO_2 laser group and from 16.90 ± 9.56 to 9.52 ± 9.73 in the itraconazole group. The mean reduction in OSI was greater in the fractional CO_2 laser group, but the difference was not statistically significant (p=0.345).

Similar trends were observed in toenail and fingernail subgroup analyses (Table 3).

Table 3: Comparison of Onychomycosis Severity Index between treatment groups

Parameter	Fractional CO_2 laser + terbinafine	Itraconazole	p-value
All nails			
OSI before treatment	17.05 ± 9.64	16.90 ± 9.56	0.941
OSI at 6 months	8.32 ± 9.70	9.52 ± 9.73	0.556
Mean reduction in OSI	8.73 ± 7.04	7.38 ± 6.61	0.345
Toenails			
OSI before treatment	18.12 ± 9.12	18.42 ± 9.08	0.890
OSI at 6 months	8.75 ± 9.38	10.50 ± 9.65	0.442
Mean reduction in OSI	9.37 ± 7.10	7.92 ± 6.08	0.358
Fingernails			
OSI before treatment	13.10 ± 10.96	12.50 ± 9.70	0.895
OSI at 6 months	6.90 ± 10.92	6.65 ± 9.55	0.955
Mean reduction in OSI	6.20 ± 6.55	5.85 ± 7.90	0.915

No serious adverse event was recorded in either group. In Group A, transient local burning or erythema was reported by a few patients during or immediately after laser therapy, but no patient discontinued treatment. In Group B, gastrointestinal discomfort was the commonest adverse effect.

One patient had transient liver enzyme elevation and was managed conservatively. Treatment completion and patient-reported satisfaction were

numerically higher in the fractional CO_2 laser group (Table 4).

Table 4: Treatment tolerability, completion and satisfaction

Parameter	Fractional CO_2 laser + terbinafine (n=20)	Itraconazole (n=20)	p-value
Treatment completed as scheduled	20 (100.0%)	19 (95.0%)	0.311
Transient local burning/erythema	3 (15.0%)	0 (0.0%)	0.231
Gastrointestinal discomfort	0 (0.0%)	4 (20.0%)	0.106
Headache	0 (0.0%)	2 (10.0%)	0.487
Transient liver enzyme elevation	0 (0.0%)	1 (5.0%)	1.000
Good/excellent patient satisfaction	18 (90.0%)	15 (75.0%)	0.407
Serious adverse events	0 (0.0%)	0 (0.0%)	-

Figure 1: Group A clinical photographs: 1) Before treatment; 2) During fractional CO_2 laser treatment; 3) After treatment.

Figure 2: Group B clinical photographs: 1) Before treatment; 2) After treatment.

Discussion

The present study compared fractional CO_2 laser combined with topical 1% terbinafine cream and oral itraconazole pulse therapy in patients with onychomycosis. Both treatment modalities produced clinically meaningful reduction in Onychomycosis Severity Index (OSI) at six months. The mean OSI reduction was numerically greater in the fractional CO_2 laser-terbinafine group than in the itraconazole group; however, the difference did not reach statistical significance. This suggests that fractional CO_2 laser combined with topical terbinafine may provide clinical outcomes comparable to oral itraconazole pulse therapy in selected patients with onychomycosis.

Onychomycosis is difficult to treat because the compact nail plate acts as a physical barrier to topical drug penetration, while slow nail growth delays visible clinical improvement. In the present study, toenail involvement was more common than fingernail involvement. This is consistent with the usual clinical pattern, as toenails grow more slowly, are more frequently exposed to repeated trauma, occlusive footwear and moist conditions, and may have relatively poorer peripheral circulation. Distal lateral subungual onychomycosis was the commonest clinical type in the present study, which is similar to the pattern reported in previous studies on onychomycosis.

The findings of the present study are comparable to those of Ranjan et al. [7], who conducted a randomized controlled trial comparing fractional CO_2 laser with topical 1% terbinafine cream versus oral itraconazole in the management of onychomycosis. In their study, fractional CO_2 laser with 1% terbinafine cream showed efficacy similar to itraconazole pulse therapy, with good safety and nail clearance. This is in agreement with the present study, where both treatment groups showed improvement, and the fractional CO_2 laser-terbinafine group demonstrated slightly greater OSI reduction, although the difference was not statistically significant.

Bhatta et al. [8] evaluated fractional CO_2 laser-assisted topical therapy in onychomycosis and reported that fractional CO_2 laser combined with topical antifungal therapy was effective in improving nail disease. Their findings support the concept that laser-assisted therapy can enhance topical antifungal penetration through the nail plate. The present study also supports this mechanism, as the laser-terbinafine group showed meaningful clinical improvement without systemic adverse effects.

Zhou et al. [9] studied fractional CO_2 laser combined with 1% luliconazole cream and reported that the combination was effective and safe in onychomycosis, with better efficacy than fractional CO_2 laser alone. This suggests that fractional CO_2 laser is more useful when combined with a topical antifungal agent rather than used as a standalone modality. The present study used a similar principle by combining fractional CO_2 laser with topical 1% terbinafine cream.

Similar results were also reported by Lim et al., [10] who treated toenail onychomycosis using fractional CO_2 laser with topical antifungal therapy and found the combination to be effective and safe. Shi et al. [11] also reported favourable outcomes using fractional CO_2 laser combined with terbinafine hydrochloride 1% cream. These studies collectively support the role of fractional CO_2 laser as an adjuvant modality that improves the delivery and action of topical antifungal agents in onychomycosis.

Arora et al. [12] assessed fractional CO_2 laser with topical 1% terbinafine cream and reported improvement in OSI following treatment. Their findings are comparable to the present study, where OSI was used as the objective measure of disease severity before and after treatment. Zaki et al. [13] compared fractional CO_2 laser plus topical antifungal therapy with fractional CO_2 laser alone and topical antifungal alone and reported better response with combination treatment. This further supports the rationale that combining laser-induced nail plate fenestration with topical antifungal therapy may produce better outcomes than either modality alone.

Itraconazole remains an established systemic antifungal option for onychomycosis. Havu et al. [14] compared itraconazole pulse therapy with continuous itraconazole therapy in toenail onychomycosis and demonstrated that pulse therapy was effective, with the advantage of reduced cumulative drug exposure. In the present study, oral itraconazole pulse therapy also produced significant clinical improvement, confirming its continued role as a standard systemic treatment option.

However, systemic itraconazole has certain limitations. It may cause gastrointestinal symptoms, headache, hepatic enzyme abnormalities and clinically relevant drug interactions. It is contraindicated in congestive cardiac failure and requires caution in patients with liver disease or polypharmacy.

These limitations have encouraged the evaluation of non-systemic, device-assisted and topical combination therapies. In this context, fractional CO_2 laser combined with topical terbinafine may be useful, especially in patients who are unwilling or unsuitable for systemic antifungal therapy. The probable mechanism of fractional CO_2 laser in

onychomycosis includes photothermal destruction of fungal elements and creation of microscopic channels in the nail plate. These microchannels may enhance the penetration of topical antifungal agents into the deeper nail plate and nail bed. In the present study, four laser sessions at monthly intervals combined with twice-daily topical terbinafine produced a slightly greater reduction in OSI than itraconazole pulse therapy. Although this difference was statistically non-significant, the absence of systemic adverse effects and better treatment completion indicate a favourable tolerability profile.

Patient-reported satisfaction was also better in the fractional CO_2 laser group. This may be due to avoidance of systemic medication, fewer systemic adverse effects and the perception of laser therapy as a targeted procedure. Transient local burning and erythema were the main local adverse effects and were self-limiting. In contrast, gastrointestinal discomfort and headache were observed in a minority of patients in the itraconazole group, and one patient had transient liver enzyme elevation. Similar tolerability observations were reported by Ranjan et al. [7], where fractional CO_2 laser with topical terbinafine was found to be effective and safe with efficacy similar to itraconazole pulse therapy.

The main limitation of the present study is the small sample size, with 20 patients in each group. Nail-level analysis was performed because some patients had multiple affected nails, but this may introduce clustering. The study was single-centre and follow-up was limited to six months. Mycological cure rates, species-wise fungal culture details and long-term recurrence after complete nail growth were not assessed in detail. Larger randomized controlled studies with longer follow-up, mycological confirmation, species identification and separate analysis of fingernails and toenails are required to confirm these preliminary findings.

Overall, the present study shows that fractional CO_2 laser combined with topical 1% terbinafine cream and oral itraconazole pulse therapy are both effective in reducing the severity of onychomycosis.

The laser-terbinafine combination showed slightly better numerical improvement and better tolerability, but without statistically significant superiority over itraconazole. Therefore, fractional CO_2 laser with topical terbinafine may be considered a promising alternative or adjunctive treatment, especially in patients where systemic antifungal therapy is contraindicated, poorly tolerated or not preferred.

Conclusion

Fractional CO_2 laser combined with topical 1% terbinafine cream and oral itraconazole pulse therapy were both effective in reducing the severity of onychomycosis over six months. The fractional CO_2 laser group showed a slightly greater reduction in OSI and better tolerability, but the difference in efficacy was not statistically significant. Fractional CO_2 laser with topical terbinafine appears to be a promising alternative or adjunctive modality, particularly for patients in whom systemic antifungal therapy is contraindicated, poorly tolerated or undesirable.

References

1. Weitzman I, Summerbell RC. The dermatophytes. Clin Microbiol Rev. 1995;8(2):240-259.
2. Karmakar S, Kalla G, Joshi KR, Karmakar S. Dermatophytoses in a desert district of western Rajasthan. Indian J Dermatol Venereol Leprol. 1995;61(8):280-283.
3. Gupta AK, Ryder JE. The use of oral antifungal agents to treat onychomycosis. Dermatol Clin. 2003;21(1):469-479.
4. Havu V, Brandt H, Heikkila H, Hollmen A, Oksman R, Rantanen T, et al. A double-blind, randomized study comparing itraconazole pulse therapy with continuous dosing for the treatment of toenail onychomycosis. Br J Dermatol. 1997;136(8):230-234.
5. Lipner SR, Scher RK. Onychomycosis: treatment and prevention of recurrence. J Am Acad Dermatol. 2019;80(7):853-867.
6. Zhou BR, Lu Y, Permatasari F, Huang H, Li J, Liu J, et al. The efficacy of fractional carbon dioxide laser combined with luliconazole 1% cream for the treatment of onychomycosis: a randomized, controlled trial. Medicine (Baltimore). 2016;95(1):e5141.
7. Ranjan E, Arora S, Sharma N. Fractional CO_2 laser with topical 1% terbinafine cream versus oral itraconazole in the management of onychomycosis: A randomized controlled trial. Indian J Dermatol Venereol Leprol. 2023;89(1):47-53.
8. Bhatta AK, Keyal U, Huang X, Zhao JJ. Fractional carbon-dioxide laser-assisted topical therapy for the treatment of onychomycosis. J Am Acad Dermatol. 2016;74(12):916-923.
9. Zhou BR, Lu Y, Permatasari F, Huang H, Li J, Liu J, et al. The efficacy of fractional carbon dioxide laser combined with luliconazole 1% cream for the treatment of onychomycosis: A randomized, controlled trial. Medicine (Baltimore). 2016;95(4):e5141.
10. Lim EH, Kim HR, Park YO, Lee Y, Seo YJ, Kim CD, et al. Toenail onychomycosis treated with a fractional carbon-dioxide laser and

topical antifungal cream. J Am Acad Dermatol. 2014;70(2):918-923.
11. Shi J, Li J, Huang H, Permatasari F, Liu J, Xu Y, et al. The efficacy of fractional carbon diox ide laser combined with terbinafine hydrochlor ide 1% cream for the treatment of onychomyc osiss. J Cosmet Laser Ther. 2017;19(5):353-359.
12. Arora S, Lal S, Janney MS, Ranjan E, Donaparthi N, Dabas R. Fractional CO_2 laser in the management of onychomycosis. J Mar Med Soc. 2020;22():50-53.
13. Zaki AM, Abdo HM, Ebadah MA, Ibrahim SM. Fractional CO_2 laser plus topical antifungal versus fractional CO_2 laser versus topical antifungal in the treatment of onych omycosis. Dermatol Ther. 2020;33(6):e13155.
14. Havu V, Brandt H, Heikkilä H, Hollmen A, Oksman R, Rantanen T, et al. A double-blind, randomized study comparing itraconazole pulse therapy with continuous dosing for the treatment of toe-nail onychomycosis. Br J Dermatol. 1997;136(12):230-234.