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Dermatology Section

Efficacy of Intramatricial Triamcinolone Acetonide versus Fractional CO_2 Laser with Topical 0.1% Betamethasone Valerate in the Management of Nail Psoriasis: A Prospective Interventional Study

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ABSTRACT

Introduction: Nail psoriasis is a refractory disease occurring in 65% of patients with psoriasis. Intramatricial steroid injections are considered as first line therapy for nail psoriasis. Laser-assisted Drug Delivery (LADD) with topical steroids helps in better drug penetration with fewer side-effects compared to other modes of treatment.

Aim: To determine and compare the efficacy of intra-matricial triamcinolone acetonide versus fractional CO_2 laser with topical betamethasone valerate 0.1% ointment in the management of nail psoriasis.

Materials and Methods: This prospective, open-labelled and interventional study was done for a period of 12 months (November 2023 to October 2024) at the Department of Dermatology Venereology Leprosy, Chengalpattu Medical College Hospital, Chengalpattu, Tamil Nadu, India. A total of 44 patients were divided into groups A and B by simple random sampling each consisting of 22 patients. Group-A patients were given intramatricial triamcinolone acetonide injection (2.5 mg/mL, 0.1 mL per session). Patients in Group-B received fractional CO_2 laser (40 mJ, 0.8 mm distance) followed by twice daily application of topical steroid. Four treatment sessions were performed at four weekly intervals. Assessment was done using modified Nail Psoriasis Severity Index (mNAPSI) score and grading of improvement at baseline, during each treatment session and at six months. Statistical analysis was done using Statistical Package for Social Sciences (SPSS) version 27.0. Significance tested using independent t-test and Chi-square test and p-value of <0.05 was considered statistically significant.

Results: Both groups showed significant improvement at the end of six months (Group-A: p<0.001; Group-B p=0.0016). 40% and 30% patients in Group-A and B, respectively showed 100% improvement but it was not statistically significant (p=0.19). Side-effects were noted in 75% and 15% of patients in Group-A and B, respectively. No recurrence was noted in six months follow-up.

Conclusion: Fractional CO_2 laser with topical betamethasone valerate 0.1% is safe, effective and convenient for patients because of fewer side-effects comparing to intramatricial triamcinolone injection. Fractional CO_2 LADD can be considered a newer modality of treatment in nail psoriasis.

Keywords: Intralesional steroid, Laser-assisted drug delivery, Nail disorder, Topical steroids

INTRODUCTION

Nail psoriasis is a refractory disease that occurs in 65% of patients with psoriasis. It can occur as an isolated disease or as a part of all types of psoriasis. It is more common in patients with extensive psoriasis, longer disease duration, family history of psoriasis and concurrent psoriatic arthritis [1].

Nail psoriasis is caused by the inflammation of the nail bed or nail matrix [2]. The nail matrix located beneath the proximal nail fold is mainly responsible for nail plate formation. Nail matrix involvement leads to clinical features like nail pitting, red lunula, leukonychia, and crumbling of the complete nail plate [3]. The involvement of nail bed, which lies directly beneath the nail plate leads to nail changes such as onycholysis, splinter haemorrhages, subungual hyperkeratosis, and subungual oil drops (salmon patches).

First-line treatment options include intralesional steroids and methotrexate injections [4]. For second-line treatment, topical steroids, vitamin D analogues, and keratolytics are commonly used. Third-line treatments involve systemic methotrexate, biologic therapies, and small molecule inhibitors [5].

The therapeutic challenge primarily arises from the unique anatomy of the nail unit, where the dense keratinised nail plate acts as a formidable barrier to drug penetration, making conventional topical therapies less effective.

Intralesional injections bypass the nail plate and directly suppress inflammation at the disease site. However, this modality is associated with significant pain during administration, technical difficulty, and potential adverse effects such as nail dystrophy and local atrophy, resulting in poor patient compliance [6].

Consequently, nail psoriasis is frequently chronic, treatment-resistant and time-consuming to manage, necessitating the exploration of more effective drug-delivery strategies [7].

Recent advances have focused on enhancing transungual drug delivery. Fractional CO_2 laser creates microscopic channels in the nail plate, facilitating targeted delivery of topical medications into deeper structures, thereby improving efficacy while minimising systemic exposure [8]. Laser-Assisted Drug Delivery (LADD) with topical therapeutics is a newer approach resulting in better penetration of topical medications and fewer side-effects [8].

Hence, the present study was undertaken to determine and compare the efficacy and safety of intramatricial triamcinolone acetonide versus fractional CO_2 laser with topical betamethasone valerate 0.1% in the management of nail psoriasis.

MATERIALS AND METHODS

This prospective, open-labelled and interventional study was done for a period of 12 months (November 2023 to October 2024) at the

Department of Dermatology Venereology Leprosy, Chengalpattu Medical College Hospital, Chengalpattu, Tamil Nadu, India after obtaining Ethical Committee approval from the institution. (IEC -CMC/approval/19/23).

Inclusion and Exclusion criteria: Patients of either sex above 18 years and below 60 years with nail psoriasis with or without skin manifestations (with Psoriasis Area Severity Index (PASI) <20 if skin involvement present), patients willing to give written informed consent were included in the study. Pregnant and lactating women, patients on anticoagulants or with bleeding and coagulation disorders, patients receiving systemic therapy for psoriasis or stopped systemic therapy for less than three months, patients with psoriatic arthritis, patients with active local infection, known peripheral arterial diseases and known hypersensitivity to drugs used in the study were excluded.

Sample size calculation: Sample size was calculated using comparison of two means formula: $n= 2\sigma^2 (Z\alpha/2 + Z\beta)^2/d^2$. Based on the mean reduction in mNAPSI score reported by Nassar A et al., assuming 95% confidence interval and 80% study power, the calculated sample size was 33 patients in total [7]. Considering feasibility constraints and an anticipated 25-30% loss to follow-up in longitudinal nail psoriasis studies, the minimum required total sample size was determined to be 44 patients, randomly divided into two groups of 22 each.

Patient demographic details such as age, gender, type of psoriasis, duration of the disease, number of nails involved, nail matrix and nail bed changes were noted. mNAPSI score was calculated. Three features (pitting, onycholysis/oil-drop dyschromia, and crumbling) of each nail are graded on a scale from 0 to 3. Four features (leukonychia, splinter haemorrhages, hyperkeratosis, and red spots in the lunula) are scored 1 if present and 0 if absent for each nail. The range of possible scores using the mNAPSI is 0 to 13 for each nail [9].

Study Procedure

Group-A patients were treated with intramatricial steroid injection. Under strict aseptic precautions, digital nerve blocks were given using 2% lignocaine in web spaces lateral to the corresponding extensor and flexor tendons. A 30 G insulin syringe was used for intramatricial injection. Triamcinolone acetonide injection (2.5 mg/mL, total volume 0.1 mL) was prepared, and 0.05 mL was injected into proximal nail matrix from the junction of proximal and lateral nail folds on both sides forming area of 'V' and confirmed by immediate blanching of lunula. All patients were given analgesics (paracetamol) twice daily for three days.

Group-B patients were anaesthetised with topical Eutectic Mixture of Local Anaesthetics (EMLA) for 45 minutes and then were treated with fractional CO_2 laser with power 25 W, duration 1.6 ms (40 mJ energy), distance of 0.8 mm passed over diseased nails once covering the proximal nail folds, followed by twice daily application of topical betamethasone valerate 0.1% till next session.

Both groups were treated at four weeks interval for maximum of four sessions.

Evaluation was done with mNAPSI score at the baseline and at the end of six months after starting therapy. Grading of improvement was used to assess the treatment response between two groups. (G0- No improvement, G1- 25-50% improvement, G2- 51-75% improvement, G3- 76-99% improvement, G4- 100% improvement) [9].

STATISTICAL ANALYSIS

Statistical analysis was done using SPSS version 27.0. Significance tested using independent t-test and Chi-square test and p-value of <0.05 was considered statistically significant.

RESULTS

A total of 44 patients participated in the study, divided into two groups of 22 patients each. Two patients from each group were lost to follow-up. For effective analysis patients who were lost to follow-up were not evaluated for tests of significance. At the end of six months of treatment, 20 patients in each group were evaluated for the degree of improvement (N=20). The general characteristics of patients in both groups are depicted in [Table/Fig-1].

Characteristics	Group-A (n=22)	Group-B (n=22)	p-value
Age (mean±SD) (in years)	41.5±9.35	40.5±10.64	0.742
Gender			
Male	11 (50%)	13 (59%)	0.60
Female	11 (50%)	9 (41%)	
Psoriasis in other areas			
Chronic plaque psoriasis	12 (54.5%)	13 (59%)	0.52
Palmoplantar psoriasis	9 (41%)	7 (32%)	
Scalp psoriasis	1 (4.5%)	1 (4.5%)	
Nail psoriasis	0	1 (4.5%)	
Number of nails involved			
1-3 nails	3 (14%)	6 (27%)	0.29
4-6 nails	13 (59%)	8 (36%)	
7-10 nails	6 (27%)	8 (36%)	
Duration			
<5 years	11 (50%)	8 (36%)	0.36
>5 years	11 (50%)	14 (64%)	
Nail changes			
Pitting	16 (73%)	18 (82%)	0.05
Leukonychia	4 (18%)	6 (27%)	
Red lunula	0	1 (4.5%)	
Crumbling	9 (41%)	6 (27%)	
Oil drop sign	5 (23%)	7 (32%)	
Sub ungual hyperkeratosis	4 (18%)	8 (36%)	
Splinter haemorrhages	2 (9%)	1 (4.5%)	

[Table/Fig-1]: Baseline characteristics of the study population (N=44).
*n=22 at enrollment; n=20 completed the study (2 lost to follow-up per group); Independent t-test was used for continuous variable and Chi-square test was used for categorical variables

There was no statistical difference in age, gender, type of psoriasis and duration of the disease between the two groups (p>0.05) [Table/Fig-1].

When comparing treatment response using mean mNAPSI score at baseline and at six months, both groups had statistically significant treatment response with p-value of <0.001** in Group-A and 0.0016* in Group-B [Table/Fig-2].

Groups	Baseline (mean±SD)	At 6 months (mean±SD)	p-value
Group-A	8.8±4.52	1.75±2.75	<0.001
Group-B	11.2±9.26	3.65±4.68	0.0016

[Table/Fig-2]: mNAPSI score.
Paired t-test used for intragroup comparison p-value<0.05 statistically significant.

When comparing the mean mNAPSI score between the two groups, mNAPSI score was 1.75±2.75 in Group-A and 3.65±4.68 in Group-B. The difference between the two groups was not statistically significant (p=0.128) [Table/Fig-3].

Groups	mNAPSI (mean±SD)	t-test	p-value
A	1.75±2.75	-1.56	0.128
B	3.65±4.68		

[Table/Fig-3]: mNAPSI score intergroup comparison.
Independent t-test was used for intergroup comparison

In Group-A, 80% of patients showed a higher grade of improvement (40% in each of G3 and G4). In Group-B, G3 and G4 improvements were observed in 20% and 30% of patients, respectively.

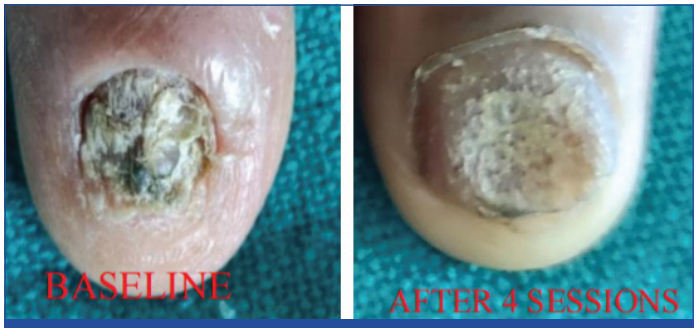
When comparing the grading of improvement between the two groups, the result was not statistically significant, with a p-value of 0.190 [Table/Fig-4].

Grading of improvement	Group-A	Group-B	Chi-square test	p-value
G0	1 (5%)	1 (5%)	3.06	0.19
G1	2 (10%)	2 (10%)		
G2	1 (5%)	7 (35%)		
G3	8 (40%)	4 (20%)		
G4	8 (40%)	6 (30%)		
Total	20	20		

[Table/Fig-4]: Comparison of grading of improvement.

Improvement in nail changes post four sessions of intramatricial triamcinolone acetonide is shown in [Table/Fig-5a,b].

[Table/Fig-5a]: Group A- intramatricial triamcinolone acetonide.
The above figure shows improvement in pitting and onycholysis after four injections of triamcinolone acetonide



[Table/Fig-5b]: Group A- intramatricial triamcinolone acetonide.
The picture shows some improvement in onycholysis and subungual hyperkeratosis after four injections of triamcinolone acetonide

The improvement in nail changes post four sessions of fractional CO_2 laser with topical betamethasone valerate 0.1% is shown in [Table/Fig-6a,b].

[Table/Fig-6a]: Group B- Fractional CO_2 with 0.1% betamethasone ointment.
The picture shows some improvement in pitting, longitudinal ridging after four sessions of fractional CO_2

[Table/Fig-6b]: Group B- Fractional CO_2 with 0.1% betamethasone ointment.
The picture shows some improvement in pitting after four sessions of fractional CO_2

Overall, 85% of patients in Group-B and 25% of patients in Group-A experienced no side-effects with significant p-value of 0.00041*. Pain was the most common side-effect in Group-A, affecting 65% of patients [Table/Fig-7].

Side-effects	Group-A	Group-B	p-value
Nil	5 (25%)	17 (85%)	0.0004
Paronychia	1 (5%)	1 (5%)	
Onychomycosis	0	1 (5%)	
Hypopigmentation	0	1 (5%)	
Pain	13 (65%)	0	
Haematoma	1 (5%)	0	

[Table/Fig-7]: Side-effects.
No recurrence noted in both groups during the study period

DISCUSSION

The prevalence of nail psoriasis is 40% (15% to 79%) of psoriasis patients. Nail psoriasis affects the quality of life and has a stigma among the patients [10]. Treatment of nail psoriasis is a time-consuming process with often unfavourable outcome and frequent relapses.

Systemic treatments for nail psoriasis alone with minimal skin and joint involvement can cause multiple systemic side-effects affecting various organs in the body. The efficacy of topical medication is limited by its penetration into the nail bed or the nail matrix. LADD has been used for other conditions successfully to enhance the penetration of topical agents limiting the use of systemic drugs [11].

Intralesional corticosteroids are considered standard therapy for matrix disease but are limited by pain and procedure-related adverse effects.

In the present study, both treatment groups demonstrated a statistically significant reduction in mean mNAPSI scores from baseline to six months. Group-A showed a decrease from 8.8±4.52 to 1.75±2.75 ($p<0.001$), while Group-B showed a reduction from 11.2±9.26 to 3.65±4.68 ($p=0.0016$), indicating significant improvement in nail psoriasis severity in both groups. A higher proportion of patients in Group-A achieved greater clinical improvement, with 80% demonstrating Grade 3 or Grade 4 response compared to 50% in Group-B. However, the difference in the grading of improvement between the two groups was not statistically significant ($p=0.190$). This lack of statistical significance may be attributed to the relatively small sample size, which may have limited the ability to detect differences between the treatment modalities despite a trend toward better clinical improvement in Group-A.

Similarly, Afify AA et al., demonstrated a significant reduction in mNAPSI when fractional CO_2 laser was combined with topical therapy, suggesting enhanced drug penetration through laser-induced microthermal channels. Their study included 20 patients with nail psoriasis. Group-A received fractional CO_2 laser followed by topical methotrexate, while Group-B received fractional CO_2 laser followed by topical calcipotriol (0.05 mg/g) plus betamethasone (0.5 mg/g). Four sessions were performed at 2-week intervals. Both

groups showed a highly significant reduction in total NAPSI scores at one month (Group-A: p<0.001; Group-B: p<0.001) and two months (Group-A: p<0.000; Group-B: p<0.001), with no statistically significant difference between the groups at baseline or during follow-up (p=0.271, 0.513, and 0.647) [12].

Hassan Moftah N et al., also reported greater improvement in mNAPSI with fractional CO_2 laser-assisted methotrexate delivery compared to methotrexate gel alone. In their study, of 36 patients with fingernail psoriasis, one hand was treated with fractional CO_2 laser at 4-week intervals along with daily methotrexate 1% gel for four months, while the other hand received methotrexate gel alone. At the end of treatment, both groups showed significant improvement in total NAPSI scores (p=0.001) with no significant difference between them (p=0.593). However, at the 3-month follow-up, the improvement in the laser-treated group was significantly greater than in the non-laser group (p=0.001), supporting the role of laser-assisted drug delivery [13].

In El-Sharkawy DA et al., study 30 patients with nail psoriasis with at least two affected fingernails were included. One affected fingernail of each patient received six sessions of fractional CO_2 laser in monthly intervals. Another affected fingernail of each patient received topical betamethasone/calcipotriol ointment once daily in addition to the monthly fractional CO 2 laser sessions. There was no statistically significant difference between the two studied groups (p >0.05) [14].

The improved safety profile observed in the present study, where 85% of patients in the laser group experienced no adverse effects compared to only 25% in the injection group, is in agreement with the findings of the study by Nassar A et al., where 36 patients with fingernail psoriasis were divided into two groups, Group-A were treated with intralesional injection of triamcinolone acetonide while Group-B received fractional CO_2 laser therapy followed by topical application of triamcinolone acetonide for six sessions. Even though no statistically significant difference was found between the two groups, fractional CO_2 laser treatment was associated with significantly lower pain scores (p=0.03) and higher patient satisfaction (p=0.007) [7].

The present study similarly indicates that combining fractional CO_2 laser with topical corticosteroid (betamethasone valerate 0.1%) is a viable and effective alternative, albeit without significantly superior outcomes compared to injectable corticosteroids.

No recurrence was observed during the six-month follow-up period in either group, similar to the study done by Starace M et al., suggesting both modalities provide sustained short-term disease control [15]. However, longer follow-up studies are required to determine durability of response.

Overall, the present study findings indicate that fractional CO_2 laser-assisted topical steroid therapy offers efficacy comparable to intramatricial steroid injections while providing significantly better tolerability, making it a useful alternative particularly in patients unwilling or unable to tolerate injections.

A notable strength of the present study is the direct head-to-head comparison of systemic (injection-based) and laser-assisted topical therapies in a parallel-group design. Unlike intra-patient or split-nail studies [11,12], the authors' approach avoids potential cross-contamination between treated and untreated nail quadrants. However, the smaller sample size and short follow-up duration remain limitations.

Overall, accumulating evidence (including our findings) suggests that Fractional CO_2 laser can serve as a well-tolerated alternative or adjunct to injectable treatments in nail psoriasis, particularly in patients where pain or procedural anxiety is a concern. Future research should aim at standardising laser protocols, exploring long-term outcomes, and comparing cost-effectiveness across modalities.

Limitation(s)

The present study was conducted with a small sample size, the calculated sample size for the study was 22 in each group; however, only 20 participants were included in the final analysis (2 patients lost to follow-up). This slight reduction in sample size may have marginally decreased the statistical power of the study and could have limited the ability to detect smaller differences. Additionally, no blinding was applied. The short follow-up period may have missed cases of delayed remission.

CONCLUSION(S)

Treatment with fractional CO_2 laser followed by topical betamethasone valerate 0.1% is effective in nail psoriasis and has fewer side-effects than intramatricial injection. Fractional CO_2 LADD can be considered a newer modality of treatment in nail psoriasis. This study supports the use of both intramatricial triamcinolone and fractional CO_2 laser with topical corticosteroids as effective treatment modalities for nail psoriasis. The choice between them may ultimately depend on patient tolerance, preference, and access to treatment facilities.

Author's contribution: Conceptualisation, Methodology, Writing-original draft, Writing- review and editing, resources was done by JV. Supervision, Validation, Visualisation was done by FS and Data curation, Formal analysis, Investigation; Project administration, Software was done by SS.

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