Fractional CO_2-assisted topical delivery of tofacitinib as an effective modality for refractory nail psoriasis

Dear Editor,

Nail psoriasis (NP) can be challenging to treat, especially in its isolated form. Patients on systemic treatment for psoriasis may require an additional topical or intralesional modality for NP. Unfortunately, there are few available and effective topical modalities for this disease. Calcipotriol and betamethasone dipropionate combination and tazarotene 0.1% are topicals that have been used for NP with variable efficacy. Topical tofacitinib, which is a Janus kinase (JAK) inhibitor, has been used in cutaneous psoriasis but very sparingly in NP.[1]

A 38-year-old male (Patient 1) presented with coarse nail pitting suggestive of nail matrix related psoriasis. Nail disease was refractory to conventional topical agents, including topical steroids and retinoids, which were given for 6 months. Patient 2 was a 44-year-old male who presented with nail matrix related psoriasis predominantly in the form of crumbling of the nail plate and coarse nail pitting. Prior treatment with conventional topical agents such as Topical tazarotene 0.1% gel and combination of clobetasol propionate 0.05% with calcipotriol 0.005% ointment was used twice daily for 6 months without improvement in nail pitting did not give adequate results. Both patients were then treated with a combination of fractional CO_2 laser and topical tofacitinib. After 45 minutes of topical anaesthesia, fractional CO_2 (Futura RF 50, Dermaindia®) treatment was administered primarily over the nail plate overlying the lunula and proximal nail fold (Power 12W, Energy 18mJ, pulse duration 1.5ms, 2 passes). Topical 2% tofacitinib ointment was applied immediately after the procedure under occlusion. The patient was advised to continue the topical treatment once daily under occlusion. Fractional CO_2 was done for a total of 3 sittings at an interval of 4 weeks. Treatment response was assessed at baseline and at each visit by modified nail psoriasis severity index (mNAPSI) scores. At 12 weeks of treatment, patient 1 showed a reduction in mNAPSI from a baseline score of 5/96 to 1/96 [Figures 1a and 1b], and patient 2 showed a reduction in mNAPSI from a baseline score of 7/96 to 3/96 [Figures 2a and 2b]. The treatment was well-tolerated in both patients with no significant adverse effects. Findings have

Figure 1a: Coarse and irregular pitting seen over nail plate with mNAPSI of 5/96 in patient 1.

Figure 1b: Marked improvement in nail matrix changes (mNAPSI-1/96) after 3 sittings of fractional CO_2 laser with topical tofacitinib 2% ointment.

How to cite this article: Agrawal A, Ramassamy S. Fractional CO_2-assisted topical delivery of tofacitinib as an effective modality for refractory nail psoriasis. Indian J Dermatol Venereol Leprol. 2026;92:106-8. doi: 10.25259/IJDVL_1807_2024

Received: November, 2024 **Accepted:** April, 2025 **Epub Ahead of Print:** July, 2025 **Published:** January, 2026

DOI: 10.25259/IJDVL_1807_2024 **PMID:** 40826882 **Supplementary data available on** https://doi.org/10.25259/IJDVL_1807_2024

Figure 2a: Crumbling and irregular pitting seen over nail plate with mNAPSI of 7/96 in patient 2.

Figure 2b: Marked improvement in nail matrix changes (mNAPSI- 3/96) after 3 sittings of fractional CO_2 laser with topical tofacitinib 2% ointment.

Table 1: Summary of clinical findings

Patient number	Patient 1	Patient 2
Gender	Male	Male
Cutaneous lesions	Yes	Yes
Systemic treatment	No	No
Nail findings	Coarse irregular pitting	Nail plate crumbling and coarse pitting
Baseline mNAPSI	5/96	7/96
mNAPSI at 12 weeks	1/96	3/96
Adverse effects	No significant adverse effects. Temporary laser marks over the nail plate	No significant adverse effects. Temporary laser marks over the nail plate

been summarised in Table 1. Dermoscopy (Heinz Delta,10x) [Supplementary Figure 1a and 1b] revealed coarse irregular pitting in patient 1 along with crumbling of the nail plate in patient 2 [Supplementary Figure 2a and 2b] which showed marked improvement after 3 sittings for fractional Co2 with tofacitinib [Supplementary Figure 1 and 2 respectively].

NP can be a difficult disease to treat. Various intralesional, topical, and systemic agents have been used for NP management. With isolated NP involving less than three nails and having only nail matrix involvement (as seen in our case), steroid or methotrexate injections are proposed to be the first line treatment modality.[2] However, they might be unacceptable to many patients due to the invasive nature of the procedure and possible pain during administration. Second-line treatments include topical agents such as steroids, retinoids like tazarotene, and calcipotriol.[2] However, penetration of topical agents to the nail matrix is hindered by the proximal nail fold, which reduces its efficacy.

Fractional CO_2 has been used in NP as a method of trans-ungual drug delivery and for the remodelling of the nail unit.[3] The depth of penetration correlates with the laser fluence and has been found to be approximately 150-200 micrometer.[4] It has also been used in combination with other topicals, including steroids, tazarotene, and methotrexate, with moderate efficacy in NP.[3,5,6] However, these agents can have side effects such as irritation of the nail folds, atrophy, and hypopigmentation.[1] We used a unique combination of fractional CO_2 with tofacitinib 2 % ointment for the management of NP. Tofacitinib is a non-specific JAK inhibitor targeting mainly JAK 1 and 3. It helps in normalise the interleukin-23/T-helper 17 axis, thereby limiting psoriatic inflammation.[1] Its enhanced penetration in two cases of nail matrix psoriasis with the help of fractional CO_2 showed good clinical efficacy. In both patients, the treatment was well-tolerated without any significant adverse effects. Fractional CO_2-assisted delivery of topical tofacitinib may be considered as an alternative therapeutic option in refractory cases of NP. Future controlled studies with a larger sample size will provide more conclusive evidence.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent.
Financial support and sponsorship: Nil.
Conflicts of interest: There are no conflicts of interest.
Use of artificial intelligence (AI)-assisted technology for manuscript preparation: The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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Rickets in congenital ichthyosis: A case report and brief review

Dear Editor,

Vitamin D deficiency remains a global health concern, particularly among children. Emerging evidence reports children with congenital ichthyosis face a greater risk with more severe deficiency, clinical and/or radiological evidence of rickets being observed in 41% of children with congenital ichthyosis against 10.8% of apparently healthy children.[1,2] The primary step of vitamin D production involves the skin; incidentally, the very organ affected in ichthyosis. Its connection to bone health might not be immediately evident, leading to undesirable consequences.

A four-year-old boy, second born from a third degree consanguineous marriage, was referred with generalised erythema and diffuse scaling since birth and bowing of legs since the last two years. The mother reported a term birth via caesarean section. At birth, a collodion membrane necessitated a ten-day neonatal intensive care admission, after which erythema and loose dry scales appeared all over his body. A history of increased redness on photo-exposure inducing an avoidance of sun and epiphora was reported. Developmental milestones were appropriate for age. There were no other mucocutaneous or systemic associations. Two years ago, the child developed pain and difficulty in walking, with subsequent bowing of lower limbs. The family had never consulted any doctors for this since infancy.

On examination, diffuse, superficial, white powdery scales and mild erythema was noted over his face with ectropion [Figure 1a]. Similar scaling without erythema was noted over the body and the extremities. Pectus carinatum [Figure 1b] and anterior bowing of bilateral lower limbs were noted. Laboratory evaluation revealed vitamin D levels <3 ng/mL, alkaline phosphatase (ALP) 1131 IU/L, parathyroid hormone (PTH) 173.9 pg/mL, and phosphate levels 3.8 mg/dL on admission. Radiological workup confirmed osteopenia, genu varum of distal femur and tibia, and severe metaphyseal changes, confirming the diagnosis of rickets [Figure 2a and 2b]. He was started on per-oral cholecalciferol 60,000 IU weekly for ten weeks and elemental calcium of 75 mg/kg/day for three months. Corrective surgery in the form of telescopic nailing with osteotomy was performed. The family was determined to continue their ayurvedic treatment and refused genetic testing, hence bland emollients were started. They were lost to follow-up post- discharge.

Vitamin D has a very close association to skin. Figure 3a shows the production, metabolism, and functions of vitamin D.[1,3,4]

Congenital ichthyoses are a heterogeneous group of disorders of cornification that are characterised by varying levels of scaling and/or erythema,[5] and hence can affect vitamin D metabolism, making them susceptible to developing rickets and osteomalacia in children and adults, respectively.[3] Vitamin D deficiency leading to hypocalcemia can present with varying amounts of extra osteal and osteal presentations. Subsequent effects on bone mineralisation are due to raised ALP and PTH levels [Figure 3b].[3,6,7]

Non-syndromic and syndromic congenital Ichthyoses have been catalogued to be associated with vitamin D-deficient

How to cite this article: Tuli S, Hegde SS, Sardesai VR, Dilkush R. Rickets in congenital ichthyosis: A case report and brief review. Indian J Dermatol Venereol Leprol. 2026;92:108-11. doi: 10.25259/IJDVL_695_2024

Received: May, 2024 **Accepted:** August, 2024 **Epub Ahead of Print:** October, 2024 **Published:** January, 2026

DOI: 10.25259/IJDVL_695_2024 **PMID:** 39508650 **Supplementary data available from:** https://doi.org/10.25259/IJDVL_695_2024