



## TREATMENT OF NAIL PSORIASIS: A REVIEW

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**ABSTRACT**

Nail involvement is an extremely common presentation in people with psoriasis, with life time incidence of nail involvement being 80-90% and is very closely associated with psoriasis vulgaris and psoriatic arthritis. Even though, 5-10% of the cases may have an isolated nail psoriasis, it is usually overlooked. Nail psoriasis has been termed as one of the difficult psoriasis, due to various problems and hurdles experienced during the treatment, like patient tolerance, bioavailability, cost of treatment or longer duration of treatment. Nail psoriasis has a significant psychosocial and economic impact on the life of the patient, as the clinical presentation can not only be painful, but also have a cosmetic disadvantage and cause hindrance in intricate and delicate work. In this review, we discuss about various clinical manifestations and the Nail Psoriasis Severity Index (NAPSI) briefly and explore in depth, the multiple treatment modalities like nail care, topical agents, phototherapy and photochemotherapy, systemic agents and the newer Biological agents and their effectiveness.

**KEYWORDS :** Psoriasis, Nail Psoriasis, NAPSI, Biologicals

**INTRODUCTION**

Psoriasis is an extremely common, chronic, multisystem inflammatory disease involving the skin and different joints in the body, which accounts for approximately 2.3 % of the total outpatients of dermatology in India <sup>(1)</sup>. Even though the skin and joint manifestations are more characteristic and significant the life time incidence of nail involvement is 80-90% and nails can be involved in 10-55% of the psoriatic patients <sup>(2,3)</sup>. <sup>(4)</sup>. Moreover, there can be an isolated nail involvement in 5-10% of the cases without any skin or joint changes <sup>(2,5)</sup>. There is a close association between nail psoriasis with high risk of psoriatic arthritis. Patients with psoriatic arthritis may have 70% prevalence of Nail involvement. In most cases, it may occur before joint involvement and may be considered as a predictor of future psoriatic arthritis as well <sup>(4, 6)</sup>. A possible reasoning behind this strong association can be the close anatomical proximity of the nail unit and the DIJ (distal interphalangeal joint). The inflammation of the tendons, joint capsule and the tendon enthesis, which are the attachment point of the ligaments, may extend and involve the nail unit causing psoriatic changes <sup>(7)</sup>.

Nail psoriasis can have different clinical presentation depending upon the structure of the nail unit involved (Table-1). Psoriasis may affect the nail matrix causing indentation or irregular nail pitting, leukonychia, red patches in the lunula and onychodystrophy. If there is nail bed involvement, it can lead to oil drop patches, splinter haemorrhage, onycholysis, subungual hyperkeratosis and parakeratosis at the same time nail fold involvement may lead to paronychia. The most common finding of nail psoriasis is the irregular nail pitting or indentations and the most severe is the 'psoriatic crumbly nail' <sup>(2,3,7)</sup>.

**Table 1- Common Clinical Findings In Nail Psoriasis**

Nail Matrix Involvement	Nail Pitting Leukonychia Onychodystrophy Nail Crumbling
Nail Bed Involvement	Oil-drop patches Splinter Haemorrhage Onycholysis Subungual Hyperkeratosis

Nail psoriasis has a significant emotional, physical and cosmetic scarring leading to an impact on the quality of life, affecting jobs, difficulty in doing intricate work, cosmetic

handicap and also in some cases, pain and altered touch sensations <sup>(8)</sup>. Though there are many different and successful treatment modalities available for psoriatic skin and joint lesions, the treatment of nail psoriasis still remains a challenge due to many different factors inclusive of attaining optimal concentration of drug at the site, the drug delivery, restricted bio-availability of drugs on site of lesions, side-effects, duration, unrealistic expectations of the patients, patient compliance and the responsiveness and severity of the disease <sup>(9)</sup>. The treatment poses a challenge when it is an isolated presentation and has been referred to, as one of the difficult locations of psoriasis <sup>(10)</sup>. Hence the Nail Psoriasis Severity Index (NAPSI) has been developed with an objective to assess the nail involvement and the treatment outcome (Table-2). The affected nail is divided into 4 quadrants, in each of which both the nail bed and nail matrix alterations are noted and scored from 0-4. All the values are added for each nail so that the maximum score is 40 for each hand or foot and the total score for all the nails ranges from 0-160. The higher the NAPSI score, worse the disease <sup>(11,12)</sup>. In a report by Mukai et al. <sup>(13)</sup> it was determined in psoriatic patients using acitretin that, although the method of evaluating the disease and its outcome by NAPSI score was rapid and easy for the clinicians on outpatient basis, it may not be able to take into consideration the minute nail changes or quantify the already existing lesions. To further increase the sensitivity of the score, a modified Nail Psoriasis Severity Index (mNAPSI) was proposed by Cassell et al. in 2007 <sup>(7,14)</sup>.

A scoring system to assess the effect of nail psoriasis on effect of life has been developed by Ortonne et al. <sup>(15)</sup> in France which consists of 10 questions called the NPQ10 score. The newest of all is the NAPPA score- Nail Assessment in Psoriasis and Psoriatic Arthritis. Being the only survey that covers various dimensions of nail involvement in isolated as well as in psoriatic arthritis patients, it has been shown to have a good patient acceptance and has been used in clinical studies and routine care <sup>(16)</sup>.

It is important to select the treatment option on the basis of the specific part of the nail involved and the specific psoriatic nail changes <sup>(2,14)</sup>. For the patients who present with isolated nail involvement, till date the first line of therapy is topical.

**GENERAL CARE OF NAILS**

Minor traumatic factors such as nail biting, manicure,

clearing subungual debris, picking or trimming the cuticle or wearing tight shoes can trigger psoriatic nail changes and so, nail protection, avoiding trauma and general nail care to avoid exacerbations, becomes a major part of the treatment of nail psoriasis. Hands and feet should be wiped dry thoroughly, nails must be kept short and physical trauma is discouraged in practice, as formation of psoriatic lesions at the site of injury is a very commonly occurring phenomenon, also known as the Koebner or isomorphic response.<sup>(5,7)</sup>

### TOPICAL THERAPY

Various topical treatment modalities have been tried successfully including corticosteroids, intralesional steroids, vitamin D<sub>3</sub> analogues, anthralin, tazarotene, 5-fluorouracil and cyclosporine.

The fundamental challenges faced by topical therapy are the fact that anti-psoriatic agents penetrate very slowly into the nail plate or not at all. Different vehicles like lacquer, tinctures, ointments and nail polish have been developed to successfully penetrate the nail plate and improve the on-site drug delivery.

#### Corticosteroids-

potent corticosteroids applied under occlusion, have traditionally been considered as the main topical treatment. Clobetasol propionate 0.05% in gel or cream or ointment form has been most widely used form of topical treatment. But various side effects like telangiectasis, depigmentation, and atrophy and bone resorption have been noted. 8% clobetasol propionate in nail lacquer was used in 45 patients with favourable benefits by Baran and Tosti<sup>(17)</sup>. The lacquer has helped to reduce the side effects usually associated with intralesional therapy or the cream or gel form of corticosteroid treatment and increase the subungual penetration and therapeutic benefits in both nail matrix and nail bed involvement<sup>(18, 19)</sup>. In a 2012 study by Nakamura et al. the efficacy of clobetasol propionate in different concentrations 0.05%, 1% and 8% was tested, which concluded with 51% reduction in NAPS I score and 8% clobetasol propionate being most effective.<sup>(20)</sup>

#### VITAMIN D<sub>3</sub> ANALOGUES-

vitamin d<sub>3</sub> analogues inhibit differentiation and growth of keratinocyte and suppress the T-cell activity and cytokine production and hence have been used in treatment of nail psoriasis<sup>(2, 18, 21, 22)</sup>. Different analogues have been in use like calcitriol, calcipotriol and tacalcitol. Local application of Calcipotriol twice daily for 3-9 months has been shown to be as effective as betamethasone propionate in reducing subungual hyperkeratosis, with side effects like periungual irritation, erythema and burning<sup>(21, 23)</sup>. Topical Vitamin D<sub>3</sub> have been known to be more effective in nail bed involvement of psoriatic nail changes and so a synergistic effect of combination of calcipotriol with a topical corticosteroid (clobetasol propionate) which acts better with nail matrix involvement was shown in a study by Rigopoulos et al.<sup>(24)</sup> and which is a safer and better alternative to a single treatment modality<sup>(18, 23, 35)</sup>

#### Anthralin-

it is an anthracene derivative with anti-proliferative and anti-inflammatory action which was used in one study by Yamamoto et al.<sup>(26)</sup> in 1998, which concluded that if used in concentration of 0.4-2% in Vaseline, once daily for 30 minutes and then rinsed with water, for a duration of 5 months showed significant improvement in 60% of the 20 patients with reduced nail pitting, onycholysis and paronychia. Nail plate pigmentation and local irritation were the main side effects observed<sup>(26)</sup>.

#### Tazarotene-

0.1% tazarotene in gel form have been used with successful

results in clinical practice<sup>(27, 28)</sup>. It is a synthetically derived retinoid from Vitamin A which downregulates the keratinocyte production, differentiation and also exhibits anti-inflammatory properties. Rigopoulos et al. in a double-blind study demonstrated that tazarotene 0.1% cream and clobetasol propionate 0.05% cream were equally effective in reducing onycholysis, pitting, discoloration and hyperkeratosis after 12 weeks in 46 patients<sup>(29)</sup>. In another randomised controlled trial in 31 patients, tazarotene 0.1% gel successfully improved onycholysis and nail pitting without any significant effect on leukonychia or splinter haemorrhages<sup>(30)</sup>. Fischer-Levancini et al<sup>(31)</sup> successfully used Tazarotene 0.1% hydrophilic ointment on 6 patients with improvement of mean NAPS I scores of 14.3 at baseline to 2.3 at the end of 5 months.

#### 5-FUOROURACIL-

extremely limited and old data is available on the use of topical 5-fluorouracil (5-FU) for nail psoriasis. It is a pyrimidine analogue. 1% 5-FU therapy in 20 patients in a study by Fredriksson et al. showed significant improvement in 17 patients with 75% reduction in symptoms<sup>(32)</sup>, but the therapy has caused aggravation of onycholysis<sup>(33)</sup>. Various other side effects like nail loss, hyperpigmentation, skin irritation, onycholysis and lack of reliable fresh data, limits its use in clinical practice.

#### Cyclosporin-

cyclosporine in oil dissolved 70% solution was used in 8 patients for 12 weeks with reduction in pitting and onycholysis in a placebo-controlled trial<sup>(34)</sup>.

### INTRALESIONAL THERAPY

#### Intralesional steroids-

especially in the case of nail matrix involvement, intralesional steroid injection have been a safe and traditional form of treatment modality. Triamcinolone acetonide 10-40mg/ml has been injected weekly or monthly<sup>(35, 36, 37, 38, 39)</sup>. Injections are given at up to 4 different sites with needles or Dermo-Jet syringes. The side effects or risk include the pain related to the injection, atrophy of proximal nail fold or even tendon rupture in some cases<sup>(2)</sup>.

One case of severe psoriatic nail disease was treated with intralesional methotrexate at a dose of 2.5mg weekly injection for 6 weeks successfully by H Saricaoglu et al.<sup>(40)</sup>

In a recent, open-label, comparative study of intramatrix injections of Triamcinolone, methotrexate and cyclosporine (Two injections at 6-week interval) for nail psoriasis, Mittal, et al.<sup>(41)</sup> reported that triamcinolone acetonide (10mg/ml) and methotrexate (25 mg/ml) groups showed more than 75 % improvement and cyclosporine (50 mg/ml) group showed only 33 % improvement after 24 weeks.

### PHOTOTHERAPY

Phototherapy with UVB and photochemotherapy with UVA in addition with psoralen (PUVA) has been a successful part of treatment for skin lesion and several studies have shown the effectiveness of the same in the treatment of nail psoriasis, although with conflicting and contradictory results. Some literature suggests that nail pitting and onycholysis exhibit poor response to PUVA<sup>(36)</sup>, on the other hand a topical PUVA therapy showed significant improvement of onycholysis and nail pitting in 4 out of 5 patients<sup>(42)</sup>. A study on penetration of UV light in cadaveric nails showed that there was minimal penetration of UVA whereas UVB was completely blocked by the nail plate<sup>(43)</sup>.

Soft x-rays in the dose of 1.5Gy for a total of 13.5Gy (43 kV, 25mA, 0.6 mm aluminium filter) at 1- and 2-week intervals was used in 1 case of very thick psoriatic nail, with complete

resolution after 12 months of therapy<sup>(44)</sup>.

Because of their proven benefits in plaque type psoriasis in recent years, photodynamic therapy (PDT) and pulse dye laser (PDL) have also been used for the treatment of nail psoriasis. In a study of 5 patients, 595nm PDL (7mm spot size, 1.5ms pulse duration, 8-10j/cm<sup>2</sup> energy) was used once monthly for 3 months with significant improvement of nail bed involvement and reduction of mean NAPSI score from 21.2 at baseline to 3 at 1 month after 3 session<sup>(45)</sup>. In a randomised, double blind, left-to-right, intrapatient study to evaluate the efficacy of PDL with two different pulse durations (6ms, 9j/cm<sup>2</sup>, 7 mm spot size versus 0.45ms, 6j/cm<sup>2</sup>, 7 mm spot size) in 20 patients, Treewittayapoom et al. found that PDL was effective in both nail matrix and nail bed lesions and there was significant reduction in mean NAPSI scores of both groups after 6 months of first treatment, without any significant statistical difference between the longer and the shorter duration of laser<sup>(46)</sup>. In an attempt to evaluate the effectiveness of PDL and PDT, Fernandez-Guarino et al. conducted a left-to-right comparison study in 14 patients with nail psoriasis. Following a 3-hour occlusion with methyl-aminolaevulinic acid (MAL) on one hand, both hands were treated with 595 nm PDL once a month for 6 months. Both the groups were found to be equally effective in both nail matrix and nail bed lesions and MAL did not play any role in the outcome<sup>(47)</sup>.

In a single blind, left-to-right, controlled study, to evaluate the efficacy and the safety of PDL along with topical retinoid for treatment of nail psoriasis, Huang YC et al. treated one hand with 595 nm PDL once a month for 6 months with 0.1% tazarotene cream (experimental hand) and the other hand (control hand) was treated only with 0.1% tazarotene cream. After 6 months of treatment, the mean decrease in the mNAPSI score from the baseline was significantly higher in the experimental hand as compared to the control hand and it was concluded that PDL with topical retinoid is a safe and effective form of treatment for nail psoriasis<sup>(48)</sup>.

In another left-to-right, controlled study to evaluate the efficacy of PDL plus calcipotriol betamethasone gel versus Nd:YAG laser plus calcipotriol betamethasone gel, Arango-Duque LC et al. concluded that both the treatment forms were equally safe and effective for both nail bed and nail matrix lesions without any statistical difference between the two and without any side effects<sup>(49)</sup>.

Kartal SP et al. in a recent study on 16 patients, found long pulsed Nd:YAG laser a promising and effective treatment option with significant reduction of mean NAPS score after 3 sessions of treatment. Both nail bed and nail matrix lesions were equally responsive<sup>(49)</sup>.

## SYSTEMIC THERAPY

After the topical or intralesional therapy has been unresponsive, systemic therapy can be warranted for the treatment of severe nail psoriasis or psoriasis vulgaris accompanied with nail changes<sup>(5,10,27)</sup>.

### Acitretin-

it is a vitamin A derivative (retinoid). A higher dose is given at the beginning which is tapered down to minimum with the course of the disease. 41% reduction of mean NAPS score with complete to near-complete resolution in 25% patient was noted by Tosti A, et al. with low dose acitretin therapy 0.2- 0.3 mg/kg/day<sup>(50)</sup>. Ricceri, et al. reported significant nail improvement with 0.5mg/kg dose of acitretin combined with urea nail lacquer after 2 months of treatment in a case of severe nail psoriasis<sup>(51)</sup>. As retinoids are known to have a significantly higher rate of side effects like hepatotoxicity, hypertriglyceridemia and are known to be teratogenic, they should only be used to treat very severe and resistant cases of

nail involvement.

### Methotrexate (MTX) -

it is a folic acid antagonist, which has been used as the primary immunosuppressive drug to treat various chronic inflammatory diseases. Since it inhibits proliferation of undifferentiated cells, it was developed to treat neoplasms. There are many side effects, mainly due to its toxicity on liver and kidneys and also a risk of bone marrow suppression with long term treatment. Parenteral administration is preferred as it is better tolerated and more effective as compared to oral administration. Gumusel et al. compared the effectiveness of methotrexate with systemic cyclosporine A. there was an average reduction of NAPS score of around 43.3% after 24 weeks of treatment with initial dose of 15mg/week with methotrexate as compared to an average reduction of NAPS of around 37.2% with cyclosporine A. In nail matrix lesions, MTX was significantly superior, whereas in nail bed lesions, cyclosporine was superior<sup>(52)</sup>. MTX is associated with a higher rate of systemic side effects like pancytopenia, dehydration, megaloblastic anaemia, nephrotoxicity, hepatotoxicity, ulcerative stomatitis, which call for stopping the therapy. Folic acid substitution can help in avoiding mild side effects<sup>(53)</sup>.

### Cyclosporine A-

it acts as an immunosuppressant by inhibiting T cell activation and decreases the release of inflammatory mediators and has been used in transplant medicine and to treat chronic inflammatory diseases. Syuto et al. reported complete remission of nail changes in 2 out of 16 patients and significant improvement in 14 out of 16 patients with systemic cyclosporine A at an initial dose of 3mg/kg/day, which was then reduced to 1.5mg/kg/day<sup>(54)</sup>. Oral cyclosporine (3.5-4.5 mg/kg/day) and topical calcipotriol cream (50mcg/kg/day) in combination, has shown to have a higher efficacy as compared to monotherapy with cyclosporine alone, in a comparative study on 54 patients by Feliciani, et al<sup>(55)</sup>. Various drug interactions should be kept in mind while administering cyclosporine as they may either increase the risk of side effects or alter with the bioavailability of the drug. It is contraindicated in patients with kidney dysfunction, infections, immunocompromised states, uncontrolled hypertension or present or past history of malignancy.

### Apremilast-

it inhibits the spontaneous production of TNF-  $\alpha$  from human rheumatoid synovial cells by selectively inhibiting phosphodiesterase 4 (PDE-4) enzyme. It is administered orally at a dose of 30mg twice a day. In a 52-week, phase 2b and 3 randomised, placebo-controlled trial to establish the efficacy of Apremilast in severe nail and scalp psoriasis, Nguyen, et al<sup>(56)</sup> reported 22.5%, 43.6% and 60.2% improvement of NAPS scores at 16, 32 and 52 weeks respectively in ESTEEM-1 patients; and 29%, 60% and 59.7% improvement in NAPS at 16, 32 and 52 weeks respectively. With only headache and diarrhoea as side effects, they concluded that Apremilast can be a safer and more convenient treatment option to treat severe scalp and nail psoriatic lesions. Rich P et al. in a phase III randomised controlled trial (RCT) reported significant reduction of NAPS scores at week 16 and week 52<sup>(57)</sup>. Kushwaha AS et al. developed a novel Apremilast Nail Lacquer formulation with penetration enhancers to improve delivery to trans-ungual and unguinal region. They reported that after 7 days of study, the concentration of Apremilast was approximately 3 folds more compared to control (without any enhancers)<sup>(58)</sup>.

### Tofacitinib-

it is a Janus kinase 1 (JAK 1) and JAK-3 inhibitor. It also inhibits the production of inflammatory mediators and suppresses STAT1- dependent gene in joint tissue. It is administered orally at a dose of 5mg twice a day. In a two 52-week, phase 3 RCT, it

was reported by Merola JF, et al. tofacitinib significantly reduced the mean NAPS I score at week 16 and maintained through week 52<sup>(59)</sup>.

## BIOLOGICALS

Introduction of biological therapy has given us a relatively safe and highly effective form of treatment option, to treat severe plaque psoriasis and psoriatic arthritis. Both antitumor necrosis  $\alpha$  (anti-TNF $\alpha$ ) and T-cell targeted therapies have been used successively, to treat severe nail psoriasis involving both the nail bed and nail matrix<sup>(7)</sup>. While there are a lot of biologicals available, Infliximab has shown to be the most effective with the strongest evidence to support the same<sup>(29,60,61)</sup>.

Biologicals have been available for the treatment of severe plaque type psoriasis and psoriatic arthritis which have also been reported to be effective in treating the nail lesions, but none of them have been officially approved<sup>(27)</sup>. The possible risk of the treatment must be carefully understood and explained, as long-term safety data regarding this class of drugs is still lacking<sup>(62)</sup>.

### Adalimumab-

it is a recombinant human IgG1 monoclonal antibody against TNF- $\alpha$  which blocks the effects of TNF- $\alpha$  by binding to the free and membrane bound TNF- $\alpha$  with high efficacy and specificity, inhibiting it from binding to receptor p55 and p75. It is administered subcutaneously at a dose of 40mg every 14 days, usually after a loading dose of 80mg. Rigopoulos et al. reported improvement of both toenail and fingernail lesions, as early as 12 weeks in a study of 21 patients treated with adalimumab for skin psoriasis and psoriatic arthritis with accompanied nail involvement. There was a mean reduction of 50% of NAPS I score and complete resolution at week 12 and 24 respectively for fingernails and toenails<sup>(63)</sup>. Van den Bosch et al. reported a mean reduction of NAPS I score by 44% at week 12 in 259 patients treated with adalimumab for nail psoriasis with psoriatic arthritis<sup>(64)</sup>.

### Alefacept-

it is a recombinant human fusion protein composed of lymphocyte function-associated antigen-3 (LFA-3) and Fc portion of human IgG. It inhibits the T-cell interaction with antigen presenting cells by binding to the CD-2 receptor present on the T-cells. It also decreases the number of pathogenic T-cells and the inflammatory response by triggering apoptosis of memory T-cells. It is administered either 15mg intramuscularly or 7.5mg intravenously every week. A little evidence is present for its use and its efficacy. Korver et al. in a study in 8 patients with alefacept reported that after 12 weeks, 3 patients showed significant improvement, 3 had no change in the nail involvement and 2 worsened<sup>(65)</sup>. Parrish et al. reported 39% reduction in NAPS I scores in 15 patients after 24 weeks of treatment<sup>(66)</sup>.

### Briakinumab-

it is a monoclonal antibody against p40 subunit of cytokines-interleukin (IL)-12 and IL-23. It is administered subcutaneously. Although not many studies have been done on this biological drug, Reich et al. in a randomised control trial in 317 patients to establish the efficacy of Briakinumab versus MTX reported significantly higher reduction of NAPS I scores with Briakinumab as compared to MTX at week 24 and 52<sup>(67)</sup>.

### Etanercept-

it is a human, soluble, TNF- $\alpha$  receptor fusion protein composed of 2 p75 components, coupled with Fc portion of a human IgG1 immunoglobulin. It inactivates TNF- $\alpha$ , by binding to TNF- $\alpha$  with greater affinity than natural receptor. It is administered subcutaneously at a dose of 50mg twice a week for 3 months, followed by once weekly thereafter. Luger et al. in a study of 711 patients reported reduction of NAPS I scored by 29% and

51% at week 12 and 54 respectively with complete resolution in 30% of the patients, being treated with etanercept for psoriasis amongst whom 80% had nail involvement<sup>(68)</sup>.

### Golimumab-

it is a human monoclonal antibody against TNF- $\alpha$ , which forms high affinity stable complexes with soluble and membrane bound TNF- $\alpha$  and thus preventing it from binding to the corresponding receptors. Kavanaugh et al. assessed the outcome of nail psoriasis in 287 patients of psoriatic arthritis, being treated with 50mg and 100mg doses subcutaneously, every 4 weeks. Significant reduction of NAPS I score was seen in both 50mg and 100mg group by 25% and 43% at week 14, and 33% and 54% at week 24, respectively<sup>(69)</sup>.

### Infliximab-

it is a chimeric, human-murine IgG1 antibody against TNF- $\alpha$ , which blocks its biological activity by binding to free and receptor bound TNF- $\alpha$ . It is administered intravenously at a dose of 5mg/kg at weeks 0, 2, 6 and repeated every 8 weeks. Bianchi et al. in the first ever study for evaluated nail severity in 25 patients being treated with infliximab for plaque type psoriasis or psoriatic arthritis. 50% reduction in mean NAPS I score was achieved at week 14 and by week 22, mean NAPS I score was 0<sup>(70)</sup>. Rigopoulos et al. in a study on 18 patients reported the reduction of NAPS I from 56 at baseline to 30 at week 14, 16 at week 22, 7 at week 30 and 3.3 at week 38<sup>(71)</sup>. In a 50-week randomised control trial with infliximab and placebo on 305 patients Rich et al. reported 26% and 57% reduction in mean NAPS I score at week 10 and 24 respectively, with complete resolution of target nail in 45% of patients by 1 year<sup>(61)</sup>. In cases of refractory, severe nail psoriasis, infliximab has been reported to be effective<sup>(72)</sup>.

### Secukinumab-

it is a human monoclonal antibody that blocks the interleukin (IL)-17A ligand and blocks the T helper (T<sub>H</sub>) 17 pathway which plays a major role in pathogenesis of a number of immune-mediated diseases including Psoriasis. In a double-blind, randomised, placebo-controlled, phase 3b trial, April W. Armstrong, et al. demonstrated the effects of Secukinumab 300mg and 150mg in patients with moderate to severe plaque psoriasis with nail involvement. At week 16 the mean NAPS I score changes were significantly higher for the groups treated with secukinumab 300mg and 150mg as compared to placebo treated group, while the only side effects reported were nasopharyngitis, headache and upper respiratory tract infections.<sup>(73)</sup>

### Ustekinumab-

it is a human monoclonal antibody blocks the biological activity of cytokines IL-12 and IL-23 by binding to its p40 subunit. It reduces the proliferation of T helper (T<sub>H</sub>)-1 and T<sub>H</sub>-17 cell population by reducing IL-17A and IL-17F. It is administered subcutaneously at a dose of 45mg if weight of the patient is < 100 Kg and 90mg if weight of the patient is > 100 Kg at weeks 0, 4 and every 12 after that. Igarashi et al. in a study of 103 patients with ustekinumab reported reduction in NAPS I scores of 45mg group and 90 mg group at week 64 as 57% and 68% respectively<sup>(74)</sup>. In a case report of 13 patients they were either treated with ustekinumab 90mg monotherapy or 45mg combination therapy with either methotrexate or oral cyclosporine A (100mg bd). Vitiello et al. reported that 38% reduction of mean NAPS I score was observed in monotherapy group after 12 weeks, whereas patients treated with combination of ustekinumab and cyclosporine A had complete resolution at week 12<sup>(75)</sup>. In a case of paradoxical psoriasis with severe nail and scalp involvement, developed after adalimumab therapy for psoriatic arthritis, ustekinumab was used with a favourable outcome<sup>(76)</sup>.

### Ixekizumab-

it is a humanized monoclonal antibody, it reduces



inflammation by selectively binding and neutralizing the cytokine IL-17A. In a phase 3 double blind trial, it was concluded with ixekizumab therapy, significant improvement in nail psoriasis was achieved and more than 50% patients showed complete resolution by week 60<sup>(77)</sup>.

### Guselkumab-

it is a human monoclonal antibody against cytokine IL-23 and mainly used in the treatment of plaque psoriasis. In a trial to assess the effectiveness of guselkumab as compared to adalimumab, it was concluded that though guselkumab showed more improvement in the psoriasis of scalp, palms and/or soles in comparison to adalimumab, whereas the magnitude of improvement of the two was same with nail involvement<sup>(78)</sup>.

### CONCLUSION

Nail psoriasis can lead to a significant amount of functional, emotional and cosmetic stress, affecting the quality of life and hence, even in isolated cases must be treated and evaluated further, as they can help predict the progression of the disease in many cases. Topical therapy and phototherapy or a combination of both must be considered as a first line treatment option and systemic or biologicals should be reserved only for very severe and refractory case. With the recent advances and ongoing trials, nail psoriasis as a solitary presentation or along with other lesions, can be effectively treated with significant improvement.

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