International Journal of Life Sciences, Biotechnology and Pharma Research Vol. 13, No. 10, October 2024 Online ISSN: 2250-3137
Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr_13.10.2024.75

ORIGINAL RESEARCH

Comparative evaluation of therapeutic efficacy and safety of 5 mg vs 2.5 mg intramatricial methotrexate in management of nail psoriasis

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Received Date: 20 August, 2024 Accepted Date: 23 September, 2024

ABSTRACT

Nail psoriasis presents a disfiguring and recalcitrant condition with varied clinical presentations. Various modalities are available such as systemic therapies like methotrexate, cyclosporine, biologicals and topical therapies in form of ultra potent topical steroids, topical retinoids etc are available.Systemic therapies such as methotrexate have yielded significant results in management of nail psoriasis along with resolution of cutaneous lesions. These are fraught with systemic side effects and often take longer duration to achieve significant improvement in nail lesions. Intramatricial therapies in form of triamcinolone acetonide,methotrexate, cyclosporine have been tried. Hence targeted therapies with minimal side effects are needed especially in patients with limited cutaneous lesions and mainly nail involvement. **Method:** We conducted a study in our institute where intramatricial methotrexate was used in doses of 5 mg and 2.5 mg. 40 patients were selected from the outpatient department of GGSMCH FARIDKOT. They were divided into 2 groups randomly using envelope method.Prior to injecting methotrexate, a distal ring block was given to minimise the pain. Baseline investigations were done before initiation of therapy and then 1 week after first injection was given.Injections were administered at base line followed by second dose at 1 week after the first and 3rd at 2 weeks after the first. NAPSI was recorded at each visit, with photographs as clinical evidence and then at 6 weeks and 12 weeks. Datawas entered in MS Excel and analysedusing SPSS 17.0 version.Patients were followed up at 6 months and 12 months, to observe any recurrence or determine the clinical improvement after cessation of therapy. **Results:** Reduction in mean NAPSI was observed in both groups with very few side effects.Difference in results between 2 groups were statistically insignificant, though the group in which 5mg of methotrexate was used showed faster onset of results. Both the doses showed similar results. Side effects were minimal apart from injection site pain. Further studies with other modalities and using different doses of methotrexate are needed to determine appropriate dosages with minimal side effects and to compare its effectiveness and safety with other modalities. Intramatricial methotrexate at low doses presents a novel approach towards managing nail psoriasis.

INTRODUCTION

Nail psoriasis affects around 32- 74 % of all the patients of psoriasis at least at one point of life (1) and isolated nail involvement can occur in 10-15% of patients. More association has been observed in patients of psoriatic arthritis. (2). It can affect nail matrix leading to pitting, beau's line, onychorrhexis,leukonychia and nail bed involvement can result in splinter haemorrhages, salmon patch.Hyponychium involvement can lead to subungual hyperkeratosis. (3). more than 20 nail pits can be diagnostic of nail psoriasis. Nail psoriasis has a profound effect on quality of life. Not only does it affect physical capacity to do work, it also can have profound psychological impact. It is resistant to conventional therapy and though intralesional triamcinolone acetonide has been very effective, methotrexate (4) when used intramatricially can also lead to resolution of lesions. In certain clinical variants such as acrodermatitis continua of hallopeau, significant nail involvement with distal phalangeal involvement occurs, and in such conditions treatment has to be done aggressively.

Historical perspective

Nail is considered as an epidermal appendage and hence its involvement in psoriasis has been well documented along with its impact.

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Treatment modalities

The most commonly recommended treatments for nail psoriasis involve the use of topical or intralesional corticoids, as well as the use of topical vitamin D3 analogues (5). Studies have shown that clobetasol propionate 0.05% in cream or gel form when used in periungual location , suffered from low absorption. A 2012 study compared the different concentrations of clobetasol propionate ,0.5 %, 1 %, 8 % showed-significant results with higher concentrations. (6).

Hydroxypropyl chitosan nail lacquer has also been used for 24 weeks. (7) Other topical treatments shown to be effective include tacrolimus, fluorouracil, topical cyclosporine, tazarotene and anthralin. Radiotherapy may be used in recalcitrant cases. However, the risk of fibrosis and malignancies must always be consideredbefore this treatment is recommended. Although phototherapy is an excellent treatment option for cutaneous psoriasis, it has not proved to be as effective for nail psoriasis. However, some evidence of the efficacy of a pulsed dye laser (595 nm) was obtained in a study of 20 patients with psoriasis.

Systemic therapies

Systemic therapies are a major modality of treatment for cases of combined skin and nail disease, use in patients who only present with nail lesions, is not recommended. According to the European Consensus for the treatment of nail psoriasis, when individuals have moderate to severe forms of the disease, methotrexate is recommended in addition to topical therapy. Tumor necrosis factor alpha inhibitors are recommended as a second line treatment (etanercept, infliximab or adalimumab).

REVIEW OF LITERATURE

Efficacy of methotrexate and cyclosporin in the treatment of cutaneous psoriasis hasbeen well established, its applicability to patients with nail psoriasis has been much less extensively studied. A randomized clinical trial comparing six-month treatments with methotrexate and cyclosporin found that both were moderately effective in treating nail psoriasis, and that their effects did not significantly differ from one another.(8)The use of acitretin in treating nail psoriasis is controversial. Studies such as that by Tosti and colleagues found this treatment to be effective, as a six-month course of 0.2 to 0.3 mg/kg/d acitretin led to a 50% reduction in NAPSI scores. Conversely, a Brazilian study conducted on 20 patients found no significant improvements after a four-month treatment course.

However, it is important to note that acitretin may cause adverse effects such as nail thinning, which may impact areas of the nail plate which have normal thickness.The recently introduced immunobiological therapy has also led to some interesting results. Infliximab is the most widely studied immunobiological agent, and has proved to be safe and effective in a year-long phase III double-blind study conducted on 378 patients with moderate to severe common psoriasis. The secondary outcome assessed by this study was the improvement of the nail condition. Infliximab was found to be superior to the placebo in this regard as early as 10 weeks into treatment, and led to growing benefits throughout the remainder of the study

.In a study conducted by Mittal et al , Intramatricial methotrexate was compared with cyclosporine and triamcinolone acetonide , it was found to be equally efficacious and with fewer side effects.(8).In a study conducted by Paras Chaudhary and others 20 patients of biopsyconfirmed nail psoriasis 2.5 mg/ml of intramatricial methotrexate was used atweekly intervals and significant reduction in NAPSI was observed.(9)

METHODOLOGY

The current study was conducted in the department of dermatologyvenerologyleprology at Guru Gobind Singh Medical college and Hospital, Faridkot Punjab after taking approval from the ethics committee.

Inclusion criteria

40 Subjects of age>18 years with nail psoriasis of 6 months duration and with or without cutaneous lesions with no history of any topical or systemic therapy in last 3 months.

Exclusion criteria

Patients undergoing systemic or any topical therapy for nail psoriasis and or the following:

- < 18 years of age, pregnancy, immunocompromised and patients of Diabetes mellitus.
- Deranged liver function tests, RFTs or known hypersensitivity to methotrexate.

40 patients of nail psoriasis with atleast 3 nail involvement were selected and randomized to two groups (group A and group B) via envelope method.C.B.C, LFTs and RFTs were done a week prior to administration of injection.

- a ring block with 0.5 mL plain lignocaine (2%) was administered in the web spaces on either side of the digit.

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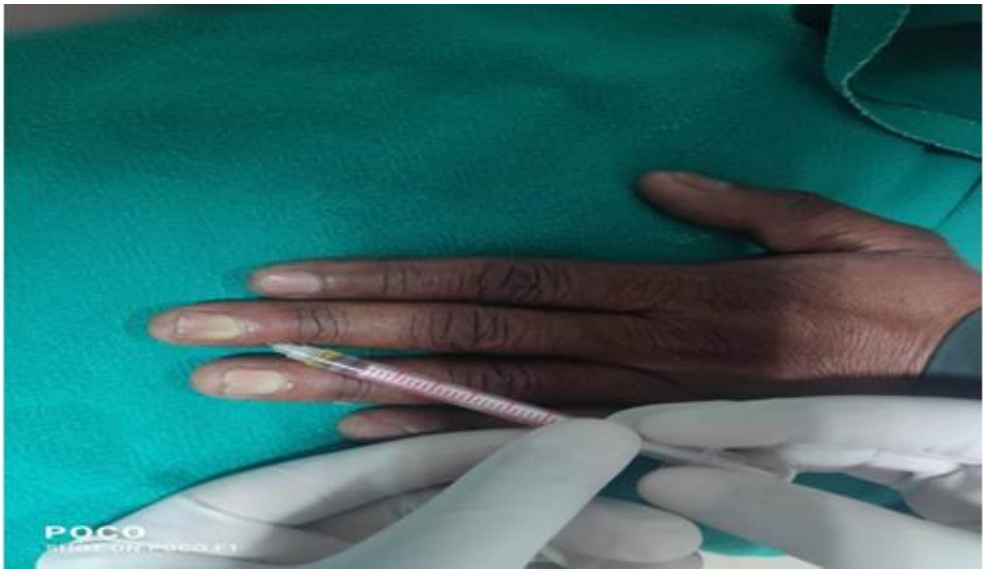
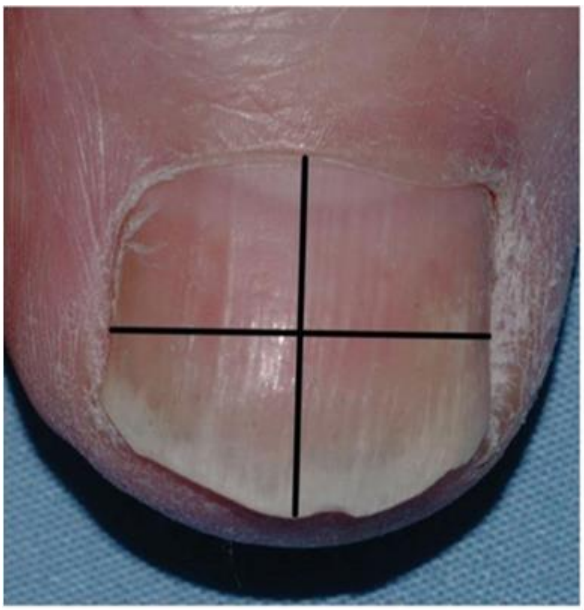


- Methotrexate 5 mg was injected intramatriciallyin the affected nails under strict asepsis in group A.
- Methotrexate 2.5 mg was injected intramatricially in the affected nailsunder strict asepsis in group B.

Investigations were repeated 2 weeks after the injection.Second dose was injected at 1 week after the first injection and 3rd at 2 weeks after the first.

NAPSI was calculated at each visit and photographic record was maintained, for this each nail is divided into four imaginary quadrants. One point each is assigned for nail matrix signs (pits, leukonychia, red spots in lunulae, crumbling,) and nail bed signs (subungual hyperkeratosis, oil drop sign, splinter hemorrhages, distal onycholysis) in every quadrant. Thus, each nail has a nail matrix score of 0–4 and nail bed score of 0–4, together making up the Nail Psoriasis Severity Index score of 0–8.

- NAPSI was calculated at 6 weeks and 12 weeks and patients were followed up for 6 months in both groups.
- Reduction in NAPSI at the above intervals were compared for both groups.



Nail Psoriasis Severity Index (NAPSI)

The target nail is graded from nail matrix psoriasis and nail bed psoriasis. The sum of these two scores is the total score for that nail.

Score for **matrix** psoriasis ____
0 = none
1 = present in 1/4 nail
2 = present in 2/4 nail
3 = present in 3/4 nail
4 = present in 4/4 nail

Nail Matrix Psoriasis consists of any of the following: pitting, leukonychia, red spots in the lunula, and nail plate crumbling.

Score for **nail bed** psoriasis ____
0=none
1 = present in 1/4 nail
2 = present in 2/4 nail
3 = present in 3/4 nail
4 = present in 4/4 nail

Nail Bed Psoriasis is the presence of absence of any of the following: onycholysis, splinter hemorrhages, oil drop (salmon patch) discolouration, and nail bed hyperkeratosis.

Total for nail _____ (0-8)

Results were measured in terms of mean NAPSI score

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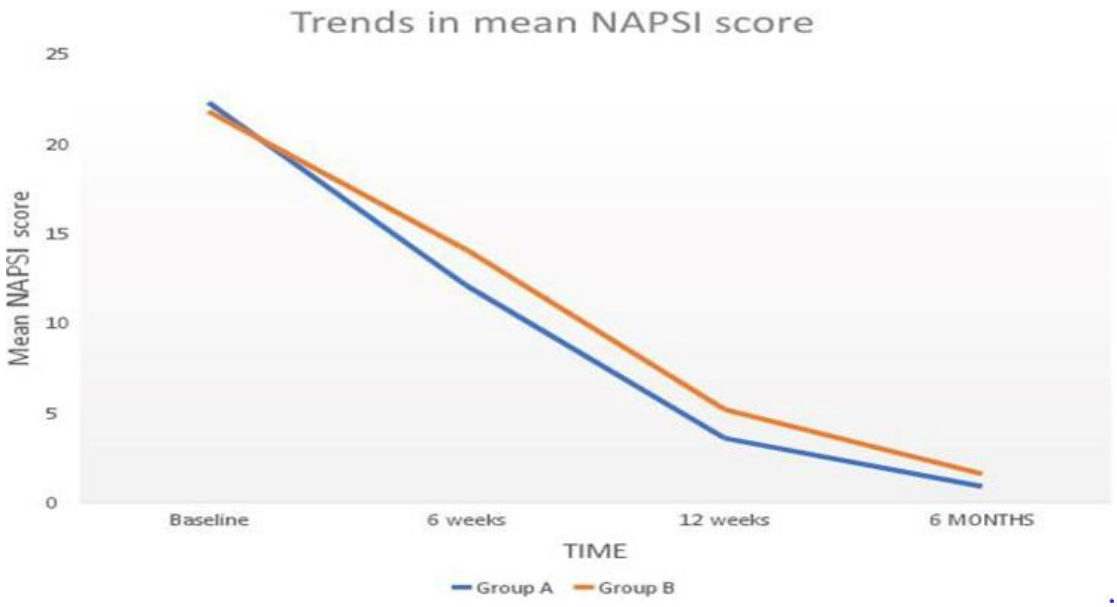
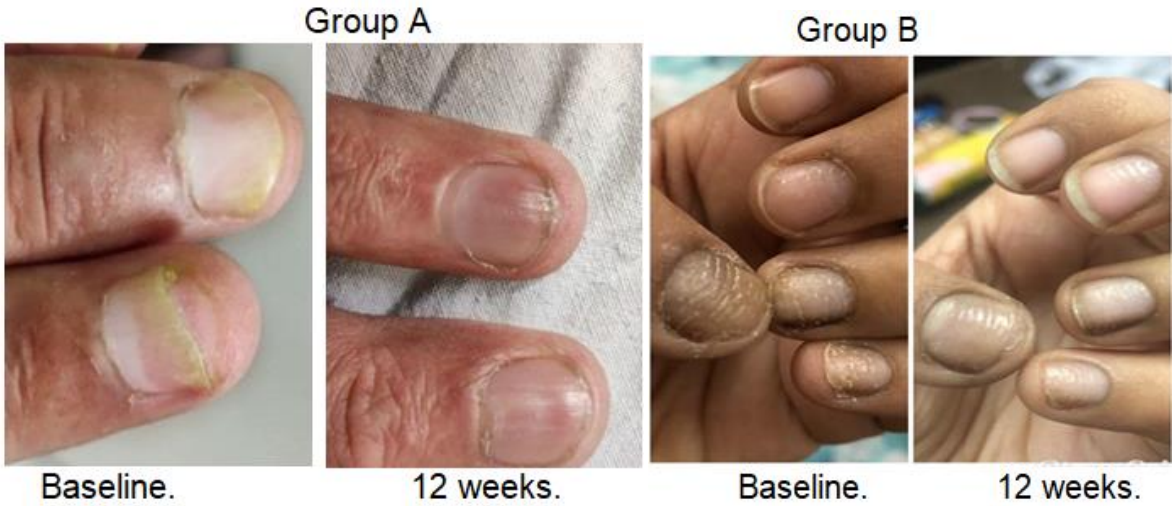


RESULTS

Time	Group A	Group B
	Mean NAPSI Score	Mean NAPSI Score
Baseline	22.300	21.800
6 weeks	12.100 (- 45 %)	14.100 (- 35%)
12 weeks	3.600 (- 84%)	5.200 (- 76%)
6 months	.900 (-96 %)	1.600 (- 93%)



Pain at injection sites was observed in 2 patients in group A and 1 patient in group B.

Both groups showed statistically significant improvement, while insignificant difference was observed between both groups statistically, still group A showed faster improvement.

DISCUSSION

Results showed that intramatricial injection of methotrexate is a safe and effective therapy for management of nail psoriasis. In other studies where intralesional methotrexate has been compared with triamcinolone acetonide, methotrexate has been found to be more effective in terms of mean NAPSI reduction. Systemic methotrexate has well known effects on improving nail psoriasis but it has its own side effects and potential systemic toxicity warrants judicious use in case very few nails are involved. More studies are needed to determine appropriate dosages of methotrexate in order to standardise the dosage. Intramatricial methotrexate presents an economical and effective modality for management of nail psoriasis with few systemic side effects.Grover et al (10) demonstrated role of methotrexate injection in nail bed in psoriasis, while our study focused on nail matrix as therapeutic target. Though topical ultra

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potent corticosteroids are useful in nail psoriasis of few nails , but prolonged use can cause bone atrophy. Intramatricial methotrexate as a treatment modality offers a safe option for managing nail psoriasis. Study conducted by Mittal et al(8) also demonstrated efficacy of intramatricial methotrexate, in comparison with intramatricial triamcinolone acetonide and cyclosporine. Our study further demonstrates efficacy of intramatricial methotrexate even in low doses, though higher doses might yield faster results. Further studies are needed to observe recurrence after stoppage of therapy if any and also placebo studies to rule out any reverse koebnerisation due to trauma of injection.

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