Intralesional Triamcinolone Acetonide Injection and Topical Betamethasone/Calcipotriol Treatment in Nail Psoriasis

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Abstract

Despite several treatment modalities, nail psoriasis is still a challenging therapeutic issue for dermatologists. Topical and intralesional steroid injections are widely used to treat psoriatic nails. Both options have shown to be beneficial for psoriatic nails with minimal or no cutaneous psoriasis. Intralesional steroid injections should be used as first-line treatment in adult patients with nail psoriasis involving just the nail matrix. On the other hand, a topical corticosteroid and vitamin D combination is the most recommended therapy for nail bed psoriasis. However, comparative studies on these therapeutic options still lack. This is a prospective pilot study that desired to study the effectiveness of intralesional triamcinolone acetonide (TA) injection and topical betamethasone/calcipotriol treatment in nail psoriasis and compare the 8 and 16-week efficacy of the treatments. There were 4 psoriasis patients with nail dystrophy who participated in the study. Each patient with 2 selected psoriatic nails was enrolled in the study (total nails = 8). The nails must have the target NAPSI score of at least 3 points. The two nails of each patient were given different treatments which were separated into group A and group B. Group-A nails received intralesional TA (10 mg/ml) injections at the 0 and 8 weeks. Group-B nails were instructed to use topical betamethasone/calcipotriol once daily for 4 months. The participants were followed up every 8 weeks to assess the target Nail Psoriasis Severity Index (target NAPSI) score and side effects. All participants were followed up for 16 weeks. At the end of the study, the mean target NAPSI score was improved by around 50% and 40% in group A and group B, respectively. Nail matrix showed more improvement than nail bed by both methods. Although, there were no significant differences in NAPSI score reduction between both treatment modalities (P>0.05), the percent improvement of the total score, matrix, and nail bed of group A were all greater than group B's score. There were no adverse events during 16 weeks except the pain while the injection process. Intralesional TA injection seems to be more effective in treating psoriatic nails than topical betamethasone/calcipotriol treatment. The injection group also shows greater efficacy in both matrix and nail bed psoriasis than topical therapy.

Keywords**:** *nail psoriasis, steroid injection, topical betamethasone/calcipotriol, nail psoriasis treatment*

1. Introduction

Psoriasis is a common chronic, immune-mediated disease with strong genetic relevance. Plaque psoriasis is the most common type found in psoriasis patients up to 80% of cases (Armstrong & Read, 2020). Patients usually present with scaly erythematous plaques on extensor surfaces, scalps, and nails. Psoriasis is associated with several comorbidities. Approximately 30% of psoriasis patients can progress to psoriatic arthritis throughout their lifespan (Armstrong & Read, 2020). Cardiometabolic disorders can also develop in severe psoriasis patients.

More than half of psoriasis patients have nail dystrophy (Jiaravuthisan, Sasseville, Vender, Murphy, & Muhn, 2007). Psoriatic nails may affect 80-90% of psoriasis patients in their lifetime (Jiaravuthisan et al., 2007). Psoriatic nail, caused by nail bed destruction, manifests hyperkeratosis, salmon patch, onycholysis, and splinter hemorrhage while nail matrix destruction can cause nail pitting, crumbling, leukonychia, red spots, and onychorrhexis (Jiaravuthisan et al., 2007). Nail psoriasis influences patients' self-esteem and it also affects patients' quality of life due to functional disablement (Augustin et al., 2010). Nail psoriasis may also be highly associated with psoriatic arthritis (Zenke et al., 2017).

There are various choices of psoriatic nail treatment. However, the exact therapeutic guideline is still controversial, and all therapeutic choices can provide little to moderate satisfactory outcomes. Systemic

drugs are considered for psoriasis patients whose extended disease. Topical and intralesional injections are more applicable modalities for nail psoriasis patients with limited disease. The most recommended treatment for a psoriatic nail with only matrix abnormality was intralesional TA injection, meanwhile topical steroid/vitamin D combination was suggested for nail psoriasis with nail bed lesion alone (Rigopoulos et al., 2019). Nonetheless, there are finite studies on the efficacy of each therapeutic way. Therefore, this study aimed to evaluate the efficacy of intralesional TA injection compared with topical betamethasone/calcipotriol for the treatment of nail psoriasis by using the target Nail Psoriasis Severity Index (target NAPSI) (Klaassen et al., 2014). Side effects were also evaluated.

2. Objectives

1) To evaluate the clinical efficacy of intralesional TA injection in nail psoriasis

2) To evaluate the clinical efficacy of topical betamethasone/calcipotriol treatment in nail psoriasis

3)To compare clinical efficacy between intralesional TA injection and topical betamethasone/ calcipotriol treatment in nail psoriasis

4) To evaluate adverse effects of intralesional TA injection and topical betamethasone/calcipotriol treatment in nail psoriasis

3. Materials and Methods

This study was done from June to December 2021 at Benchakitti Park Hospital. The study protocol has been approved by the Ethical Committee, of Thammasat University. Four patients aged 20 to 60 years with at least 2 psoriatic fingernails participated in this clinical trial. Systemic therapies, pregnancy, lactation, and topical nail treatment 2 weeks prior to the study were all excluded.

Participants' demographic data were collected at baseline including age, gender, underlying disease, type of psoriasis, and drug allergy. The specific detail of psoriasis was recorded including the disease onset, PASI score, and current medication. All fingernails were photographed by digital camera and dermoscopy. The nails were scored by using target NAPSI and 2 nails that had at least 3 points of target NAPSI were selected. The score was counted by splitting a nail into 4 quadrants. One quadrant is equal to 1 point. Each nail characteristic was counted 0-4 depending on the number of quadrants. All participants with a total of 8 psoriatic fingernails were selected.

Each nail was matched to a different group randomly by a computer generator. A nail (group A) was injected TA (10mg/ml) 0.05 ml/site 2-4 sites at week 0 and week 8. If the nail involved either nail bed or nail matrix, total injection sites will be 2 sites at nail bed or nail matrix respectively. If the nail involved both nail bed and matrix, total injection sites will be 4 sites at both nail bed and nail matrix. The digital nerve block was performed with 2% lidocaine HCL before TA injection. In another selected nail (group B), participants were instructed to apply topical betamethasone/calcipotriol ointment (Daivobet®) once daily for 16 weeks.

The assessment of both treatment regimens was performed at baseline, 8 weeks, and 16 weeks by using target NAPSI and recording adverse effects. Digital photographs and dermoscopic photos were also taken at each follow-up visit. Wilcoxon's signed-rank test was used to compute and compare the difference between the two group's target NAPSI scores.

4.1 Results

The demographic data of the subjects was shown in table 1. There were 4 patients (8 nails), 3 males and a female who completed the study. The patients had a mean age of 57.5 ± 12.92 years. All of them were plaque-type psoriasis. The patients had a mean duration of disease of 12 years.

Table 1 Demographic data of the subjects

	N=4
Gender (M: F)	3:1
Age (year)	57.5±12.9
Psoriasis type (%)	

	N=4
• Plaque-type psoriasis	100
Duration of disease (year)	12.7±5.9

The mean total target NAPSI at the baseline of group A and group B were 10.25±2.98 and 10.75±4.03, respectively, which was no statistically significant difference (*P*=0.414), see Table 2. The most common nail abnormality in both groups was leukonychia while nail crumbing was not seen in both groups. After 8 and 16 weeks of the treatments, the target NAPSI scores of both groups were diminished see, Figure 1. In Group A, the mean total target NAPSI score decreased from 10.25±2.98 to 5.5±4.79 at 8 weeks and decreased to 5±4.76 at 16 weeks. In Group B, the mean total target NAPSI score decreased from 10.75±4.03 to 7.5±4.65 at 8 weeks and decreased to 6.5±6.13 at 16 weeks Compared with the baseline, the target NAPSI score reduction of group A was not statistically significant after treatment at 8 and 16 weeks (*P*=0.102, *P*=0.068 respectively). However, the percent reduction of group A from 0 to 8 weeks was 46.3% and reduced 51.2% from 0 to 16 weeks. Group B showed 30.2% and 39.5% reduction of the target NAPSI score from 0 to 8 and 16 weeks, respectively. The reduction of the target NAPSI score of group B did not significantly change after treatment at 8 and 16 weeks (*P*=0.157, *P*=0.102 respectively). When comparing the total target NAPSI score between group A and group B, the scores did not show a significant difference at 8 and 16 weeks (*P*=0.066, *P*=0.102 respectively). However, the mean total score of group A showed a greater reduction at 8 and 16 weeks than group B's score, see Figure 1.

When separating the target NAPSI score into matrix and nail bed, all psoriatic nails had more scores of matrix abnormality than the nail bed's score at the baseline. The Target NAPSI matrix score of group A decreased from 7.00±2.70 to 3.5±3.41 at 8 weeks and 3.25±2.98 at 16 weeks. The target NAPSI reduction did not show a significant change at 8 and 16 weeks (*P*=0.109, *P*=0.068 respectively). However, when calculating to percent reduction, the scores of group A declined 50%, and 53.5% after 8 and 16 weeks of the treatment period, respectively. In group B, the target NAPSI matrix score decreased from 7±3.36 to 5.25±3.30 at 8 weeks and 4±3.91 at 16 weeks. The scores reduction, however, was not significantly different when compared with the baseline. The percent reduction was also lesser than group A at both 8- and 16-weeks follow-up, see Figure 3. Although, the matrix score comparing between-group was not statistically different at 8 and 16 weeks (*P*=0.059, *P*=0.180 respectively), group A shows a greater score reduction at 8 and 16 weeks than group B's matrix score.

The target NAPSI nail bed score of group A was 3.25±0.50 at the baseline and reduced to 2.00±1.82 and 1.75±2.06 at 8 and 16 weeks, respectively. The percent reduction of group A's nail bed score was 38.4% at 8 weeks and 46.1% at 16 weeks. In the meantime, the target NAPSI nail bed score of group B was 3.75±1.70 at the baseline and decreased to 2.25±2.06 at 8 weeks and 2.50±2.38 at 16 weeks. The percent reduction of group B's nail bed score was 40% at 8 weeks and 33.3% at 16 weeks. The mean score reduction of group A was higher and group B at both 8 and 16 weeks, see Figure 3. However, there were no significant differences between groups A and B at 8 and 16 weeks (*P*=0.317, *P*=0.180, respectively)

4.2 Discussion

There are several therapeutic options that have been used to treat nail psoriasis. Nevertheless, intralesional steroid injection and topical steroids with vitamin D are the mainstay treatment. This study aimed to evaluate the efficacy of both treatment modalities and compare by using the target NAPSI score (Klaassen et al., 2014).

Intralesional TA injection is a recommended drug to treat nail psoriasis. Several studies suggested intralesional TA injection for the first-line therapy (Bleeker, 1974 ; Boontaveeyuwat, Silpa-Archa, Danchaivijitr, & Wongpraparut, 2019; de Berker & Lawrence, 1998; Gerstein, 1962). A dermatologist and nail expert group consensus strongly recommended intralesional TA injection for a psoriatic nail with few nails involvement and limited to nail matrix (Rigopoulos et al., 2019). Every 4-8 weeks, the injection should be repeated. In this study, the group A nails were injected by TA (10mg/ml) twice at 0 and 8 weeks. The

percent reduction of the target NAPSI score was 51.2% at 16 weeks which was by the study of TA injection in 2014 (Nantel-Battista, Richer, Marcil, & Benohanian, 2014).

Table 2 Mean of target NAPSI scores of both groups at the baseline, 8-, and 16-weeks follow-up period

	0	8	16	reduction (%)	
				0 vs 8	0 vs 16
Total target NAPSI score					
Group A	10.25±2.98	5.50±4.79	5.00±4.76	46.3 (p=0.102)	51.2 (p=0.068)
Group B	10.75±4.03	7.50±4.65	6.50±6.13	30.2 (p=0.157)	39.5 (p=0.102)
p-value	0.414	0.066	0.102		
Target NAPSI matrix score					
Group A	7.00±2.70	3.50±3.41	3.25±2.98	50 (p=0.109)	53.5 (p=0.068)
Group B	7.00±3.36	5.25±3.30	4.00±3.91	25 (p=0.102)	42.8 (p=0.109)
p-value	1.000	0.059	0.180		
Target NAPSI nail bed score					
Group A	3.25±0.50	2.00±1.82	1.75±2.06	38.4 (p=0.180)	46.1 (p=0.157)
Group B	3.75±1.70	2.25±2.06	2.50±2.38	40 (p=0.083)	33.3 (p=0.131)
p-value	0.414	0.317	0.180		

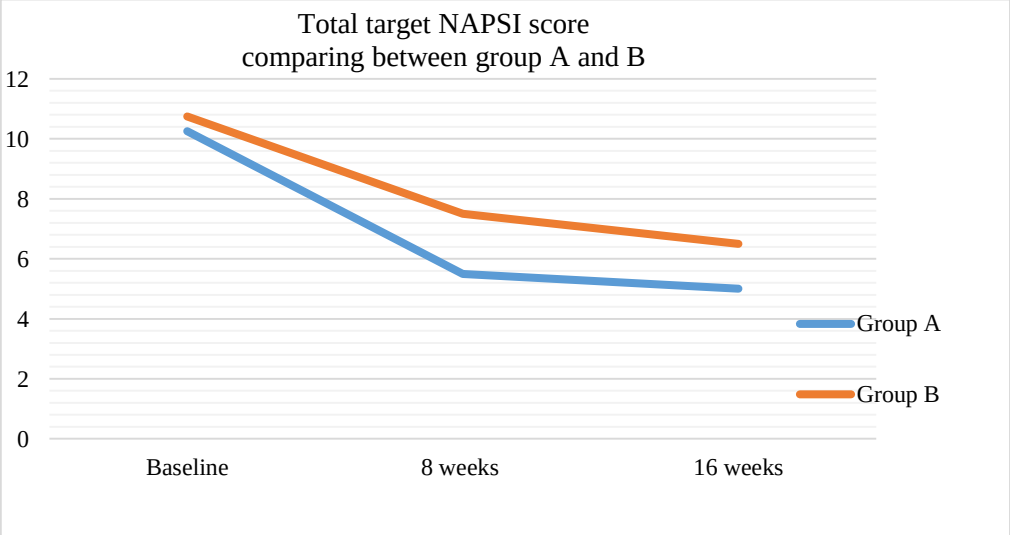

Figure 1 Total target NAPSI score at baseline, 8, 16 weeks of both groups

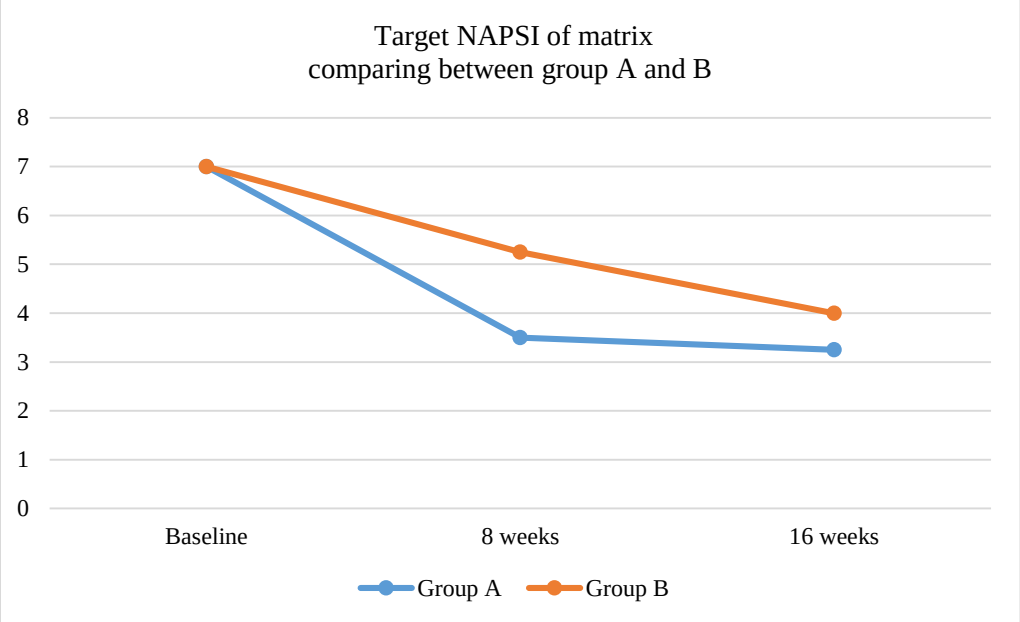

Figure 2 Target NAPSI of the matrix: comparing groups A and B

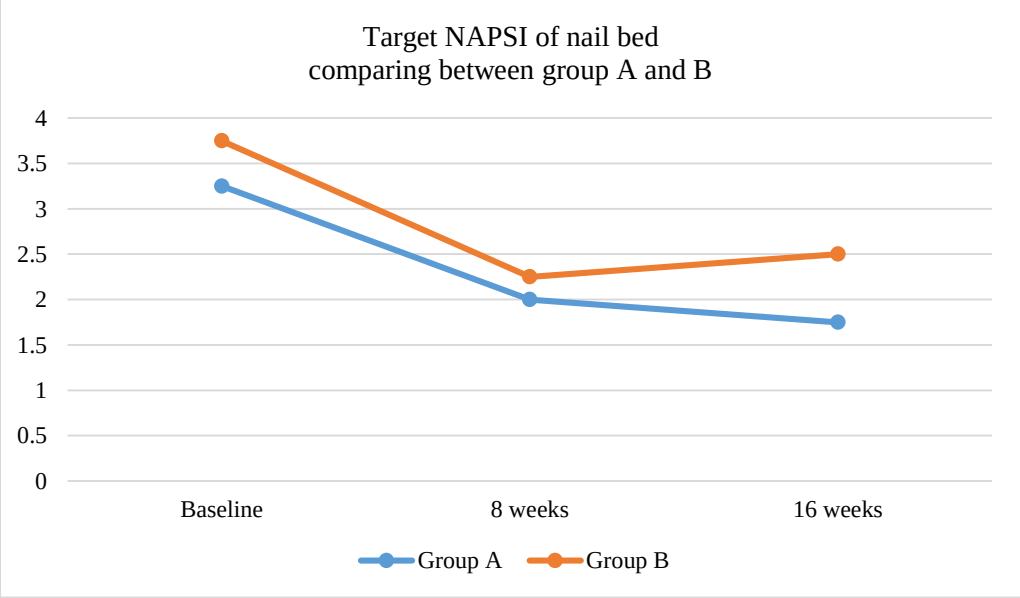

Figure 3 Target NAPSI of nail bed: comparing between groups A and B

The TA injection group showed a greater reduction of total target NAPSI scores than the topical group at both 8 and 16 weeks. In addition, the injection group also presented a higher reduction of matrix score than topical treatment. The predominant outcome of the TA injection group might be explained by the better penetration of the injection method than the topical drug. However, topical treatment is a more practical way to treat nail psoriasis. Topical steroids, topical vitamin D analogs, and topical retinoids are frequently used in the disease. (Bianchi, Soda, Diluvio, & Chimenti, (2003); Brandi, Starace, Alessandrini, Bruni, & Piraccini, (2018); Kole, Cantrell, & Elewski, (2014); Rigopoulos, Gregoriou, & Katsambas, (2007); Zakeri, Valikhani, Mortazavi, & Barzegari, (2005). However, the combination of super-potential topical

corticosteroid plus vitamin D analogues may provide an exceeding result (Rigopoulos, Ioannides, Prastitis, & Katsambas, (2002); Tzung, Chen, Yang, Lo, & Chen, (2008); Rigopoulos et al., (2009). Dimitrios Rigopoulos and nail expert dermatologists (2019) suggested topical steroid/vitamin D combination as a first-line treatment in psoriatic nails involving mainly the nail bed. Nonetheless, super potent steroids should be used for a limited period and no more than once daily because of the side effects. In this study, the participants were instructed to apply betamethasone/calcipotriol combination drug once daily for 4 months continuously. The topical therapy showed a reduction of the total target NAPSI score 30.2% at 8 weeks and 39.5% at 16 weeks. However, the TA injection treatment showed a greater improvement than the topical group. The injection therapy seemed to be more effective than the topical option according to poor absorption of the topical drug through the hard keratin of the nail plate. Nevertheless, all patients complained the painful at the nail bed during injection despite prior digital nerve block performing. Concerning the side effect, topical treatment might be more applicable than injection for nail bed lesions.

When using Wilcoxon signed-rank test to analyze the effectiveness between TA injection and topical therapy, there was no statistical difference in total target NAPSI score after treatment at 8 and 16 weeks. This insignificant result can be explained by the limited number of participants. It may be since this study was conducted during COVID-19 situations. Therefore, it must proceed under the pandemic preventive measures. Moreover, there is no control group to compare the treatments. As a result, in further study, a larger number of participants and a control group are needed to confirm the result.

All participants were satisfied with the result. One of the participants wants to continue intralesional TA injection after the study. Other participants desired to continue the topical drug. During the study, no adverse effects were recorded except the pain during injection. There were no side effects from topical betamethasone/vitamin D treatment after 16 weeks follow-up.

5. Conclusion

Intralesional TA injection and topical steroid/vitamin D are recommended for a patient who has nail psoriasis with little to no psoriatic skin lesion. Both therapeutic ways can improve the nail lesion. However, intralesional TA injection seems to be more effective than topical betamethasone/calcipotriol treatment. Both target NAPSI scores of the nail matrix and nail bed lesions decreased more in the injection treatment. Nonetheless, larger studies are needed to confirm its effectiveness.

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