A Comparison of The Effects of Clobetasol 0.05% and Photodynamic Therapy Using Aminolevulinic Acid With Red Light in the Treatment of Severe Nail Psoriasis

Zohreh Tehranchinia¹, Nasibeh Barzkar¹, Seyed Mohammad Riahi², Marjan Khazan*²

¹Skin Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
²Social Determinants of Health Research Center, Department of Epidemiology and Biostatistics, Faculty of Health, Birjand University of Medical Sciences, Birjand, Iran

Abstract

Introduction: The treatment of nail psoriasis is often difficult and unsatisfactory due to therapy resistance. This study aimed to compare the efficacy of clobetasol 0.05% ointment and photodynamic therapy (PDT) using aminolevulinic acid (ALA) and red light in the treatment of severe nail psoriasis.

Methods: This open-trial study included 69 nails of 8 patients with severe nail psoriasis. Thirty-four nails were treated with clobetasol 0.05% ointment and 35 nails were treated with ALA-PDT. ALA-PDT treatment was performed every 3 weeks for 5 cycles; the nails were treated with clobetasol under occlusion every day during the study. All the patients were followed up after 24 weeks. The severity of nail involvement was measured by the Nail Psoriasis Severity Index (NAPSI) scores at the baseline and during the treatment.

Results: There were no significant differences in the NAPSI scores between the treatment groups in the baseline and weeks 3, 6 and 9 (all \( P > 0.05 \)), although significant differences were found in weeks 12, 15 and 24 (follow-up) \( P < 0.001 \). A significant time-effect improvement was found in all the nail-matrix, nail-bed and total NAPSI scores in both treatment groups (all \( P < 0.001 \)). The patients did not report intense pain and discomfort during irradiation.

Conclusion: Clobetasol 0.05% ointment seems to be effective in treating nail psoriasis after a treatment period of 15 weeks. However, the efficacy of ALA-PDT at a 24-week follow-up was greater than that of clobetasol.

Keywords: Nail psoriasis; Photodynamic therapy; Aminolevulinic acid; Red light; Clobetasol.

Introduction

Psoriasis is a common chronic inflammatory skin disorder with nail involvement, which is mostly estimated to be 80% of psoriatic patients during lifetime⁴; however, psoriasis can just be limited to the nails in 5%-10% of cases.² On the basis of the nail structure, the clinical manifestations are mainly due to the involvement of nail matrices, such as pitting, leukonychia, and ridging. In addition, they can be because of the involvement of nail beds, including oil drop patches, onycholysis, splinter hemorrhages, and subungual hyperkeratosis.³ It has been shown that nail changes in patients with nail psoriasis are associated with cosmetic problems, interference with work, and pain, which may consequently lead to a negative impact on the quality of life.²⁴⁵ Additionally, nail psoriasis can be considered as a predictor of psoriatic arthritis.⁴ Therefore, although nail psoriasis treatment can be challenging and unsatisfactory due to therapy resistance, safe and effective treatments are required to improve the quality of life and reduce the risk of psoriasis-triggering diseases.³ It has been shown that due to the limited efficacy of the topical therapies in nail psoriasis because of the low penetrability of the topical therapies in the nail matrix and nail bed,³ phototherapy as a systemic therapy may be effective in nail psoriasis.⁷ Recently, photodynamic therapy (PDT) with 5-aminolevulinic acid (ALA) as a photosensitizer has been shown to be effective in treatment for some skin diseases, including sebaceous hyperplasia, acne, and psoriasis.⁸⁻¹¹ PDT with red light may improve the permeability of the nail bed and nail matrix by using ALA, which is metabolized to protoporphyrin IX and accumulation of ALA-induced protoporphyrin IX can be...
PDT in the treatment of plaque-type psoriasis, there are not enough previous studies that show the effectiveness of PDT in nail psoriasis. Consequently, the present study aimed to assess and compare the clinical efficacy of clobetasol propionate 0.05% ointment and PDT using ALA and red light in the treatment of nail psoriasis.

Materials and Methods

Study Protocol

The right hand as an experimental group was treated with ALA and red light-PDT, and the left hand as a control group was treated only with clobetasol propionate 0.05% ointment, which was massaged into the nail bed and covered with an occlusive dressing to increase its efficacy for 15 weeks every day. First, the nail lesions of the right hand were sealed with 20% ALA gel (MEDAC GmBH Hamburg) for 3 hours to induce the accumulation of protoporphyrin IX, as a photosensitizing agent, in the nail that was confirmed by UV irradiation. Then, PDT with the red-light source (PDT 1200, Waldmann Medizintechnik, Villingen-Schwenningen, Germany) was applied one time at a wavelength of 630 nm (range 600–730 nm) with a total dose of 120 J/cm² and an intensity of 200 mW/cm² for approximately 20 minutes. This treatment was performed every 3 weeks for 5 sessions. Follow-up evaluation was done 24 weeks after the last treatment session. To reduce and manage pain during irradiation, a mini hand-held fan was used near to the site of treatment.

Statistical Analysis

The Shapiro–Wilks test was used to assess the normal distribution. The Student's t test was used to compare the groups. The differences between the last treatment session and 24-week follow-up in both groups were determined by the paired-samples t test. Repeated measurement analysis of variance was used to compare the mean of the NAPSI score during the treatment. When the Mauchly's test of sphericity showed the heterogeneity of covariance, the Greenhouse-Geisser correction was performed to adjust the degrees of freedom in the F-tests. All statistical analyses were done by the SPSS 22.0 version, and statistically significant results were considered as \( P < 0.05 \).

Results

From a total of 69 severe psoriatic nails, 35 were treated with ALA-PDT and 34 with clobetasol propionate 0.05% in a group of 8 patients with a mean age of 32.23 ± 5.49.

The mean of the nail matrix, the nail bed, and the total NAPSI scores at the baseline and in weeks 4, 8, 15 (end of treatment), and 24 (follow-up) are shown in Figure 1.

No significant differences were found in the mean of total NAPSI scores between the two groups at the baseline and in weeks 3, 6, and 9 (\( P = 0.862, P = 0.915, P = 0.698, P = 0.695 \) respectively) (Figure 1a); there were also no significant differences in nail bed and nail matrix NAPSI scores between the two treatment groups at the baseline (\( P = 0.466, P = 0.389 \) respectively) and in weeks 3 (\( P = 0.240, P = 0.314 \) respectively), 6 (\( P = 0.234, P = 0.513 \) respectively), and 9 (\( P = 0.477, P = 0.751 \) respectively) (Figure 1b and 1c). However, statistically significant differences were observed in all three scores in weeks 12 and 15 (\( P < 0.001 \)) between the treatment groups.

The repeated measurement analysis of variance with a Greenhouse-Geisser correction showed that during the treatment period, a statistically significant reduction was found in the means of nail matrix, nail bed and total NAPSI scores in the treatment groups (all \( P < 0.001 \)) (Figure 1); a significant time-effect improvement was also found in all three scores in both groups (all \( P < 0.001 \)). The mean of total NAPSI score between two groups at the baseline and the 15-week was statistically significantly different (\( F = 8.472, P = 0.005 \)).

The mean NAPSI scores in nails treated with ALA-PDT significantly decreased from 5.97 ± 1.29 at the baseline to 4.29 ± 1.44 in week 15 and 2.11 ± 1.27 at the end of week
24 of follow-up ($P < 0.001$). Clobetasol in the treatment of nail psoriasis showed a significant reduction in the mean NAPSI scores from the baseline ($6.03 \pm 1.47$) to week 15 of treatment ($2.50 \pm 1.05$) ($P < 0.001$) and an increase in the mean NAPSI scores from $2.50 \pm 1.05$ in week 15 to $3.94 \pm 0.95$ in the follow-up ($P < 0.001$) (Table 1). There were also significant differences in the means of the nail matrix and nail bed scores from the baseline to the end of treatment and in the follow-up in both groups ($all P < 0.001$).

At the end of the 15-week treatment period, the mean NAPSI was reduced to $2.50 \pm 1.05$ presenting a 58% improvement in the clobetasol group and $4.29 \pm 1.44$ presenting a 28% improvement in the ALA-PDT group.

At the 24-week follow-up after the last treatment session, the mean NAPSI score was significantly greater in the nails treated with ALA-PDT than in the nails treated with clobetasol ($P < 0.001$) (Figure 2).

None of the patients reported intense pain and discomfort during irradiation.

**Discussion**

The results of this study showed significant differences in the mean NAPSI scores between ALA-PDT and clobetasol 0.05% ointment at weeks 12, 15 and 24. Clobetasol has been shown to be more effective in the treatment of severe psoriatic nails than ALA-PDT, although the treatment efficacy at a 24-week follow-up was significantly greater in the nails treated with ALA-PDT compared with the nails treated with clobetasol.

The incidence of nail psoriasis is reported among approximately 50% of patients and consequently can cause a decreased quality of life among them.$^{1,2,4,5}$ Nail psoriasis could also potentially be related to the risk factor in psoriatic arthritis.$^6$ First line therapies are often topical treatments, although their efficacy in nail psoriasis is limited due to the low penetrability of the nail bed and nail matrix.$^3$ However, the effectiveness of topical therapies on the nail plate may be increased under occlusion.$^{16}$ The clobetasol propionate at a concentration of 0.05% is the most common topical agent in the treatment of psoriasis.$^{17}$ The long-term use of clobetasol propionate is associated with adverse effects such as skin atrophy, telangiectasia, depigmentation and bone reabsorption.$^{18}$ Although it has been shown that clobetasol 0.05% in cream/gel/ointment generally has poor efficacy in the treatment of nail psoriasis due to limited penetration,$^{16}$ Rigopoulos et al showed the significant efficacy of clobetasol 0.05% cream in improving nail psoriasis 12 weeks after treatment.$^{19}$ Similarly, in this study, clobetasol propionate 0.05% ointment was shown to significantly improve nail psoriasis after a 15-week treatment period. However, Nakamura et al found a significantly positive effect of clobetasol propionate 8% on nail lacquer, when compared the efficacy of clobetasol at different concentrations of 0.05%, 1%, and 8% in patients with nail psoriasis.$^{20}$ These contrasting findings are probably due to different

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**Table 1. The Nail Psoriasis Severity Index (NAPSI) Scores During the Treatment and the Follow-Up Period**

<table>
<thead>
<tr>
<th>Week</th>
<th>PDT-Treated Nails (n=35)*</th>
<th>Clobetasol-Treated Nails (n=34)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Bed</td>
</tr>
<tr>
<td>0 (baseline)</td>
<td>5.97±1.29</td>
<td>3.83±0.85</td>
</tr>
<tr>
<td>3</td>
<td>5.80±1.25</td>
<td>3.80±0.86</td>
</tr>
<tr>
<td>6</td>
<td>5.57±1.13</td>
<td>3.71±0.92</td>
</tr>
<tr>
<td>9</td>
<td>5.23±1.39</td>
<td>3.51±1.01</td>
</tr>
<tr>
<td>12</td>
<td>4.80±1.38</td>
<td>3.20±1.10</td>
</tr>
<tr>
<td>15</td>
<td>4.29±1.44</td>
<td>2.83±0.95</td>
</tr>
<tr>
<td>24 (follow-up)</td>
<td>2.11±1.27</td>
<td>1.34±0.87</td>
</tr>
</tbody>
</table>

Abbreviation: PDT, photodynamic therapy.

All variables represent Mean ± SD. *P values < 0.05 were considered significant.
due to resistance in therapy and/or slow response to the treatment because of slow-growing nails, which can be affected by age and nutrient deficiency. Thus it requires long-standing treatment that might increase the risk of medication side effects. On the other hand, there is no standardized treatment for nail psoriasis and the selected treatment is dependent on multiple factors such as the history of the patient, age, sex, severity, the duration of nail psoriasis, concomitant diseases and medications, and the risks and benefits of therapy. Furthermore, systemic treatment is not recommended in psoriatic patients with only nail manifestations; it is suggested in patients with skin or joint involvement or patients resistant to treatment.16

For these reasons, in this study, it seems that ALA and red light-PDT might be an effective and safe therapeutic choice for the treatment of severe nail psoriasis due to long-term effects (at the end of follow-up) without discomfort and severe pain during treatment and any side effects.

Our study has some limitations. This study had a small sample size and was not randomized and double-blind. In addition, growing nails are strongly associated with nutrients intake that was not assessed in the patients using the Food Frequency Questionnaire.

Conclusion
After the last treatment session, the mean NAPSI scores in the nails treated with clobetasol 0.05% ointment were significantly less than those in the nails treated with ALA-PDT; however, 6 months after the last treatment session, the mean NAPSI scores in the nails treated with ALA-PDT were greater than those in the nails treated with clobetasol 0.05% ointment. Treatments were also well tolerated and none of the patients complained of discomfort during the sessions except slight pain. Additional studies using a larger number of patients are needed to confirm these results.

Ethical Considerations
The informed consent forms were taken from all patients. The study protocol (identifier: IRCT2015112825271N1; https://www.irct.ir/trial/21161) received approval from the Ethics Committee of Shahid Beheshti University of Medical Sciences (Ethical Code: IR.SBMU.SRC.REC.1394.1).

Conflict of Interests
The authors declare no conflict of interest.

References


