Evaluation of the Efficacy of Acitretin Therapy for Nail Psoriasis

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Objective: To evaluate the therapeutic efficacy of acitretin in patients with isolated nail psoriasis.

Design: Open study involving 36 patients with moderate to severe nail psoriasis treated with acitretin.

Setting: University-based outpatient dermatology clinic specializing in nail diseases.

Patients: A total of 27 men and 9 women (mean age, 41 years) with nail psoriasis.

Intervention: Therapy consisted of acitretin, 0.2 to 0.3 mg/kg/d, for 6 months.

Main Outcome Measures: Clinical evaluation, and Nail Psoriasis Severity Index (NAPSI) and modified NAPSI scores before therapy, every 2 months during therapy, and 6 months after treatment.

Results: The mean percentage of reduction of the NAPSI score after treatment was 41%; the mean percentage of reduction of the modified NAPSI score of the target nail was 50%. Clinical evaluation at 6 months showed complete or almost complete clearing of the nail lesions in 9 patients (25%), moderate improvement in 9 (25%), mild improvement in 12 (33%), and no improvement in 6 (11%).

Conclusion: Results from low-dose acitretin therapy show NAPSI score reductions comparable with those studies evaluating biologic drugs for nail psoriasis and suggest that low-dose systemic acitretin should be considered in the treatment of nail psoriasis.

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Nail involvement occurs in up to 78% of patients with psoriasis, is more common in patients with psoriatic arthritis, and may be the only sign of psoriasis.1,2 Nail psoriasis usually involves several nails, and both fingernails and toenails may be affected.

The quality of life of patients with severe nail psoriasis is affected as a result of pain and poor cosmetic appearance, subsequently leading to restricted activities of daily living.3

Signs that are highly suggestive for nail psoriasis include irregular pitting, salmon-colored patches on the nail bed, and onycholysis with erythematous borders. These signs are more commonly seen in fingernails, where several signs are often associated. Nail psoriasis often produces other nail abnormalities, including splinter hemorrhages, nail-bed hyperkeratosis, nail thickening and crumbling, paronychia, and, rarely, leukonychia, erythema of the lunula, and trachonychia. These signs are not diagnostic for nail psoriasis because they are commonly observed in other inflammatory, traumatic, or infective nail conditions.4,6

The Nail Psoriasis Severity Index (NAPSI) has been designed and successfully implemented to grade the severity of psoriatic nail disease based on these clinical findings.7 Moreover, the utilization of the NAPSI score and a modified version of this severity index score as an instrument to monitor response to therapy has been recently documented8 in the medical literature. Although nail psoriasis is common, the results of treatment of nail psoriasis are often disappointing, and unfortunately there is little information addressing the efficacy of systemic therapies in patients with diffuse and severe nail involvement in the absence of skin disease. We present herein our experience on the efficacy of low-dose acitretin in isolated nail psoriasis.

METHODS

This open study involved 36 patients with moderate to severe psoriasis limited to the nails treated with low-dose acitretin from January 2005 through January 2007. All patients gave their informed consent to participate in the study. The study was approved by the ethical committee of the Istituto Fisioterapici Ospitalieri, in Rome, Italy. The patients included 27 men and 9 women ranging in age from 28 to 67 years (mean age, 41 years). Diagnosis was based on the presence of diagnostic nail signs on fingernails (irregular pitting, salmon-colored patches, and onycholysis with erythematous border).
The NAPSI scores\(^7\) ranged from 10 to 46 (mean, 31.5); the modified NAPSI score for the most severely affected fingernail\(^8\) ranged from 4 to 11 (mean score, 7.6). Although toenails were affected in 32 patients, the severity of toenail psoriasis was not scored.

None of the patients had skin or symptomatic arthropathic psoriasis. Duration of nail abnormalities ranged from 17 to 48 months (mean, 18 months). We did not treat premenopausal women; patients with hepatic, renal, or metabolic diseases that contraindicated utilization of oral retinoids; and patients with positive findings from potassium hydroxide wet mount or cultures for fungi.

None of the patients had previously received systemic treatment for nail psoriasis. Previous topical treatments included calcipotriol hydrate, steroids, and tazarotene. Acitretin was given at a dosage of 0.2 to 0.3 mg/kg/d for 6 months. Patients agreed not to use topical treatment during the study. Laboratory investigations and clinical evaluation, which included photographic records, were performed every 2 months. Investigator evaluation was performed using a score on a scale of 0 (no improvement) to 3 (cleared or almost cleared). Treatment satisfaction by patients and tolerability were assessed at each visit. All patients were followed up for at least 6 months after the end of treatment.

**RESULTS**

The mean NAPSI score at the end of the study was 18.6 (range, 6-34); the mean modified NAPSI score for the target nail was 3.8 (range, 1-6). The mean percentages of reduction of the NAPSI score and modified NAPSI score were 41% and 50%, respectively. Clinical evaluation at 6 months showed complete or almost complete clearing of the nail lesions in 9 patients (25%), moderate improvement in 9 (25%), mild improvement in 12 (33%), and no improvement in 6 (11%) (Figure 1 and Figure 2). Patients' perception of treatment efficacy was high in 11 patients, moderate in 10, low in 3, and absent in 8 cases. The differences of values in the NAPSI score and in the mean modified NAPSI score for the target nail before and after 6 months of treatment correlated well with the clinical evaluation score. In particular, the 9 patients who were cured or almost completely cured had mean percentages of reduction of the NAPSI score and modified NAPSI score of 76% and 73%, respectively. Both scores, however, are very sensitive and detect minimal signs of nail psoriasis. This explains why patients who were considered to be clinically cured did not achieve a 100% reduction of the scores (Figure 1 and Figure 2).

Only 1 of the 36 patients experienced adverse effects on the nail during treatment. This patient, a 49-year-old woman receiving acitretin at a dosage of 0.3 mg/kg/d, experienced severe dryness of the periungual skin and multiple pyogenic granulomas 2 months after beginning treatment, which required lowering the dosage to 0.2 mg/kg/d. None of the patients had to interrupt treatment because of drug-related clinical or laboratory adverse effects.

Follow-up showed recurrence of nail psoriasis after interruption of treatment even though the mean NAPSI and
modified NAPSI scores for the target nail at the evaluation performed 6 months after treatment were lower than those at the beginning of the study (NAPSI score, 26.8; modified NAPSI score for the target nail, 6.5). All patients who were improved did not return to pretreatment conditions.

**COMMENT**

Treatment of isolated nail psoriasis is difficult and often unsatisfactory. Information about the efficacy of systemic treatments on nail psoriasis is scarce because most studies on skin psoriasis do not focus on the nail changes. Retinoids have been reported to be effective in a few studies, but, to our knowledge, their efficacy has never been assessed using objective evaluation methods.9,11 Effects of etretinate and acitretin on nail psoriasis strongly depend on dosages because these drugs may produce worsening of nail psoriasis with paronychia and nail fragility when used at the dosages recommended for skin psoriasis.12 Our results show that low-dosage acitretin is well tolerated because none of our patients experienced fragility or paronychia during treatment and only 1 patient developed periangual pyogenic granulomas (which promptly regressed after reducing the drug dosage). Data addressing the therapeutic efficacy of biologic drugs on nail psoriasis are still limited, however; in the studies referenced herein, the evaluation of efficacy was based on standardized methods (NAPSI score).13-18 Drugs that seem more effective in the treatment of nail psoriasis are adalimumab and infliximab. The mean percentages of reduction of the NAPSI score were 56%13 and 57%,18 at 24 weeks for infliximab, and 69% at 20 weeks for adalimumab.14

In our study, we assessed nail psoriasis severity using 2 different methods: the NAPSI score and the modified NAPSI score for the target nail. The NAPSI score evaluates presence of signs on the nail bed (of onycholysis, salmon patches, and nail-bed hyperkeratosis) and on the nail matrix (pitting, leukonychia, and crumbling) in all 20 nails, providing a maximum score of 80. This score does not provide information on the severity of involvement in each single nail but rather reflects the overall severity of nail psoriasis. The modified NAPSI score for the target nail scores severity of nail matrix and nail-bed psoriasis from 0 (no sign) to 3 (severe involvement) in each nail quadrant, providing a maximum score of 24. In our study, we found a very good correlation between these 2 scores in grading disease severity. We also considered the NAPSI score for a target nail because this was evaluated in some studies of biologic agents to simplify investigator assessment. Available information indicates that adalimumab and infliximab are quite effective, producing more than a 50% reduction of the NAPSI score after 20 weeks of treatment.9-10 Our results with acitretin are comparable with those because we observed a 46% reduction of the NAPSI score for the target nail at 20 weeks.

Although more studies are required to thoroughly assess the effectiveness in larger controlled subject populations, our observations suggest that low-dose systemic acitretin should be considered in the therapeutic armamentarium in the treatment of nail psoriasis.

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**Author Contributions:** All authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Tosti and Piraccini. Acquisition of data: Tosti, Cameli, and Piraccini. Analysis and interpretation of data: Tosti, Ricotti, Romanelli, and Piraccini. Drafting of the manuscript: Tosti and Piraccini.

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**REFERENCES**


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