

Therapies for Psoriatic Nail Disease. A Systematic Review

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ABSTRACT. Nail involvement is common in patients with psoriasis and psoriatic arthritis, affecting 80%–90% of patients at some time. It also has significant effects on quality of life. Psoriatic nail disease can be refractory to treatment, and different features may respond variably to different therapies. The lack of standardized outcome assessments hinders the interpretation of available data. In this systematic evidence-based review of the literature, we assess various treatments for psoriatic nail disease. (First Release May 15 2006; J Rheumatol 2006;33:1452–6)

Key Indexing Terms:

PSORIATIC ARTHRITIS

PSORIASIS

NAIL

TREATMENT

INTRODUCTION

Psoriatic arthritis (PsA) is a chronic inflammatory arthropathy characterized by the association of arthritis and psoriasis. There is substantial heterogeneity in both the extent and type of articular and dermatologic involvement. Nail involvement is common, estimated to affect 80%–90% of people with PsA at some time during their lives¹. It has been suggested that nail lesions occur more commonly in PsA than in uncomplicated psoriasis². Nail psoriasis significantly affects quality of life; one study of 1728 psoriatic patients found that 93% with nail psoriasis considered it to be a cosmetic handicap, 48% reported that it interfered with their jobs, and 52% described pain³.

Psoriasis can affect all components of the nail^{4,7}. The nail plate is composed of hard, translucent, dead keratin. The matrix, at the proximal end of the nail, synthesizes 90% of the nail plate⁴. Four epithelial structures surround the nail plate: the proximal nailfold, the matrix, the nail bed, and the hyponychium⁵.

Psoriasis of the matrix includes pitting, leukonychia, red spots in the lunula, and nail plate crumbling⁸. Pits are sharply defined depressions in the plate caused by the shedding of nail plate cells, much the same way psoriatic scale is shed⁴. Superficial pitting is produced by parakeratosis or temporary ineffectual keratinization in the proximal matrix, while deeper lesions in the nail such as smooth-surfaced leukonychia come from a parakeratotic focus in the middle matrix⁵. Crumbling (gross alteration of the nail plate surface) results from extensive matrix involvement, causing the nail to lose structural integrity^{4,5,7}.

The nail bed, which gives rise to the inferior surface of the nail plate, can manifest psoriatic disease as “oil drop” discoloration, onycholysis, nail bed hyperkeratosis, or splinter hemorrhages⁸. Oil spots are local separations of the nail plate from bed⁴. There are marked confluent parakeratosis, small Munro microabscesses, and an accumulation of periodic acid-Schiff-positive glycoprotein material in the horny layer, apparently derived from severe underlying dermal inflammation and edema with exudation⁵. Splinter hemorrhages are small extravasations of red blood cells in the dermal ridges that lodge between the epidermis and nail plate and are dragged as the plate streams distally^{5,7}. Onycholysis is separation of the nail from the nail bed beginning at the distal groove, often with accumulation of yellow, scaly debris that elevates the nail plate^{4,7}. Both onycholysis and subungual hyperkeratosis reflect psoriasis of the hyponychium with silver parakeratotic scale and absent granular lesion, similar to what is seen in psoriatic skin lesions⁵.

Compared with skin psoriasis, nail bed psoriasis has the same layering of parakeratosis and polymorphonuclear leukocytes in the stratum corneum, but has more spongiosis in the epidermis and more serum accumulation in the stratum corneum⁵. Nail disease can be refractory to treatment, and different features can respond variably to different treatments.

In our review, we assess the clinical effect on signs, symptoms, and quality of life and the toxicity of therapies for nail psoriasis in patients with PsA. Given the limited number of studies on nail disease in PsA, the search was broadened to include nail disease in patients with psoriasis, but not necessarily PsA.

Search Strategy
A comprehensive literature search of PubMed beginning in 1953 and limited to articles in English was performed. Titles, abstracts, and reference lists of selected trials were manually reviewed to identify additional studies.

Inclusion criteria: Psoriatic nail involvement in adults with psoriasis or PsA, clinical trials of agents for psoriatic nail disease, and for completeness, case series and observational studies.

Exclusion criteria: Studies or case reports with 5 or fewer

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patients, studies in which the number of patients was not clearly indicated.

Outcome Measures

There are no validated outcome tools for nail involvement with psoriasis. This and the lack of appropriate controls for many of the studies precluded meaningful determination of effect size or other quantitative assessments.

RESULTS

Using the MeSH terms “psoriatic arthritis” and “nail” and “treatment” we retrieved 19 articles. Crossing “psoriasis” and “nail” and “treatment” yielded an additional 148 articles. Twenty-one articles that met the inclusion and exclusion criteria are included in this review and are summarized in Table 1. Toxicities were reported variably; therefore we were unable to compare them. Several reported treatments (e.g., topical cyclosporine³⁰, electron beam radiation³¹, grenz ray treatment³², superficial radiotherapy³³) were not included in this review because they are not widely available.

Treatment Recommendations

Based on our interpretation of the data presented here, treatment recommendations are listed below.

- Topical steroids⁹⁻¹¹
 - Alone: marginal response, grade C⁹
 - With salicylic acid: moderate response, grade C¹⁰
 - With topical calcipotriol: moderate response, Grade B¹¹
- Topical tazarotene: moderate improvements in some features of psoriatic nail disease, grade A, C^{12,13}
- Topical urea/propylene glycol (Belanyx): improvement of nail disease, grade A¹⁵
- Topical 5-fluorouracil^{14,15}
 - Alone: improvements of nail disease, grade C^{14,15}
 - In combination with topical urea/propylene glycol (Belanyx): does not result in further improvements than Belanyx alone, grade A¹⁵
- Topical calcipotriol^{9,11,20}
 - Alone: moderate improvements, grade B, C^{9,10}
 - With topical steroid: moderate response, grade B¹¹
 - With oral cyclosporine: moderate response, grade B²⁰
- Topical anthralin^{16,21}
 - Alone: moderate improvement, grade C¹⁶
 - After oral cyclosporine or etretinate: maintains and may increase improvements with those medications, grade B²¹
- Intravenous infliximab: improvement, grade A, C^{18,19}
- Intramuscular alefacept: some improvement, grade C¹⁹
- Oral cyclosporine^{20,21}
 - Alone: some benefits, grade A, C^{20,21}
 - With topical calcipotriol: further benefits, grade C²⁰
- Oral retinoids^{9,21}
 - Alone: moderate improvement in pustular nail psoriasis, grade C^{9,21}

- Followed by anthralin: some improvement, grade B²¹
- Oral nimesulide: marginal improvements, grade C⁹
- Injectable steroids²²⁻²⁸
 - With needle and syringe: possible moderate benefits, but utility is questioned given side effects, grade C²⁶⁻²⁸
 - With needle-less device: possible moderate benefits, more for nail matrix disease; questionable side effects, grade C²²⁻²⁵
- Oral photochemotherapy: moderate benefits, grade C²⁹

DISCUSSION

The lack of data on nail involvement in PsA studies requires that data be extrapolated from psoriasis studies. Interpretation of the data is difficult: Many studies have small patient numbers, most lacked appropriate controls, and no standard outcome measures were used, making it impossible to compare outcomes.

Recently, a psoriatic nail grading instrument, the Nail Psoriasis Severity Index (NAPSI) was developed to evaluate nail matrix disease (pitting, leukonychia, red spots in the lunula, and nail plate crumbling) and nail bed disease (oil drop discoloration, onycholysis, nail bed hyperkeratosis, and splinter hemorrhages)⁸. Validation of this instrument and modified versions of the NAPSI are in progress³⁴.

Many of the trials reviewed had positive outcomes, but have questionable utility, in our opinion, because of side effects or the transient nature of the results.

Although there is a paucity of data regarding quality-of-life benefits of these therapies, patients report that psoriatic nail disease significantly affects their lives in terms of cosmetics, pain, and activities of daily living³. In one study, 77% of patients indicated they would like to undergo treatment for nail psoriasis³. Further investigations into safe, efficacious treatments for nail psoriasis are needed.

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Table 1. Treatments for nail disease.

Study	Agent	No. of Patients	Study Type	Outcome Measure	Results	p
Piraccini ⁹	Topical steroid vs topical calcipotriol (5µg/g) vs oral retinoid (etretinate 0.5 mg/day or acitretin 0.5 mg/day) vs oral nimesulide (100 mg bid)	46 total (topical steroid: 18; topical calcipotriol: 15; oral retinoid: 12; oral nimesulide: 13)	Obs	Responder or nonresponder	Topical steroid: 4/18; calcipotriol: 9/15; oral retinoid: 6/12; oral nimesulide: 4/13	
Tosti ¹⁰	Topical calcipotriol (50 µg/g) vs topical betamethasone dipropionate (64 mg/g) and salicylic acid (0.03 g/g)	56	RCT	Nail thickness (mm) measured qmo	Calcipotriol: 41–49% reduction at 5 mo in responders; betamethasone dipropionate and salicylic acid: 52% reduction at 5 mo in responders	< 0.0001 c/w baseline; 2 treatments equally effective
Rigopoulos ¹¹	Topical calcipotriol + clobetasol propionate	62 (48 w/nail disease)	Open	Hyperkeratosis thickness	72% and 70% reduction in nail thickness (fingers and toes, respectively)	
Scher ¹²	Topical tazarotene 0.1% gel	31	RCT	7-point scale for pitting, onycholysis, subungual hyperkeratosis, leukonychia, nail plate crumbling, splinter hemorrhages, nail bed discoloration	Improved onycholysis in occluded at wk 4 & 12; improved pitting at wk 24 in occluded	≤ 0.05 for those listed
Bianchi ¹³	Topical tazarotene 0.1% gel	25	Open prospective	Visual assessment scale (0–2), specific (onycholysis, hyperkeratosis, oil spots, pitting) and nonspecific (thickened/brittle nails, paronychia, splinter hemorrhages) signs	Specific signs improved statistically significantly; nonspecific signs improved	< 0.0001
Fredriksson ¹⁴	1% topical fluorouracil	20	Open prospective	Improvement	17/20 improved; decreased pitting and hypertrophy (about 75% improvement c/w baseline); nail loss seen in treated pts w/onycholysis	
De Jong ¹⁵	1% topical fluorouracil in Belanx (urea, propylene glycol) lotion vs topical Belanx lotion alone	57	RCT	Nail area severity score (0–4 score for pitting area, number of pits, subungual keratosis, onycholysis, oil spots) & overall nail severity scores	Percent improvement with: fluorouracil: 32%/40% at wk 12/16; belanx: 39%/46% at wk 12/16	≤ 0.05 c/w baseline, no difference between 2 treatment groups
Yamamoto ¹⁶	Topical 0.4–2.0% anthralin in petrolatum followed by topical 10% triethanolamine	20	Open prospective	Fair (> 50%), little (< 50%), no improvement	Improvement in: onycholysis: 4/7 pts: fair; thickening: 3/6 pts: fair; pitting: 4/8 pts: fair; longitudinal and transverse lines: none	
Reich ¹⁷	Infliximab (5 mg/kg IV) at wks 0, 2, 6 and q8 wks thereafter vs placebo at wks 0, 2, 6, 14, 22, and crossing over in double-blind fashion to infliximab (5 mg/kg IV) at wks 24, 26, 30 and q8 wks thereafter	378 (w/nail psoriasis: placebo: 65; infliximab: 240)	RCT	Nail psoriasis severity index (NAPSI) ⁸ at wks 10, 24, 50 (target nail divided into quadrants, scored for presence of 4 nail matrix and 4 nail bed features)	Percent improvement in NAPSI score: Wk 10: infliximab 26.0%, placebo –5.9%; wk 24: infliximab 56.3%, placebo –3.2%; wk 50: infliximab 56.3%, placebo crossing to infliximab 72.5%	Wk 10: < 0.0001; Wk 24: < 0.0001
Bianchi ¹⁸	Infliximab (5 mg/kg IV) at wks 0, 2, 6, 14, 22	9 psoriasis pts; 16 arthropathic pts	Open prospective	NAPSI ⁸ at wks 0, 2, 6, 14, 16, 22	Steady improvement of NAPSI score in both groups; wk 22 mean NAPSI score in both groups was 0	At wk 22 < 0.0001

Table 1. Continued.

Study	Agent	No. of Patients	Study Type	Outcome Measure	Results	p
Cassettey ¹⁹	Alefacept (15 mg IM) qwk × 12 wks	12 (only 6 w/nail psoriasis)	Open	NAPSI ⁸ ; 30% improvement at 12 wks	At 12 wks, 3/6 pts w/≥ 30% improvement NAPSI score	
Feliciani ²⁰	Oral CsA vs oral CsA w/topical calcipotriol (50 μg/g)	54	Single-blind comparative	Improvement on 3-point scale based on area involved	Improvement at 3 mo: combined: 79% pts; alone: 48% pts	Combined treatment: < 0.004; CsA alone: < 0.15
Mahrle ²¹	Oral CsA (2.5 mg/kg/day) at 10 wks, followed by oral CsA taper or topical anthralin vs oral etretinate (0.5 mg/kg/day) at 10 wks, followed by topical anthralin	210 (66.5% pts w/ nail involvement)	RCT	4-point scale	Improvement in score at 10 wks (no statistically significant difference): CsA: 17.5% (90/137 improved); etretinate: 9.2% (47/60 improved); reduced score after second phase: CsA/CsA: 46.0%; CsA/anthralin: 26.2%; etretinate/anthralin: 24.1%	< 0.01 c/w baseline for CsA/CsA group
Abell ²²	Needle-less-injected triamcinolone acetonide (5 mg/ml) 0.1 ml × 1–10 qwk × 3	7	Open	Improvement	5/7 improved	
Abell ²³	Needle-less-injected triamcinolone acetonide (5 mg/ml) 0.1 ml qwk × 2–4	24 matrix only, 20 matrix & onycholysis, 14 onycholysis only	Open	Improvement	21/24 improved (matrix only); 19/20 combined improved (matrix features more); 3/14 good results (onycholysis only)	
Bleeker ²⁵	Needle-less-injected triamcinolone acetonide q2-3 wks × 3	92 (569 nails)	Open	Cure, improvement, status quo	In 225 pts w/ involvement of matrix only, 197 w/improvement (86 recur); in 155 pts w/ onycholysis only, 81 w/ improvement (49 recur); In 167 pts w/involvement of matrix and onycholysis, 155 w/improvement in matrix and 78 w/improvement in onycholysis; 5/19 pts w/ improvement in thickened nails (3 recur)	
Bedi ²⁶	Injected triamcinolone acetonide qmo (0.1 ml of 10 mg/ml) using needle	7	Open	Graded improvement 0–3 (none to complete recovery)	4/7 complete recovery but relapsed (3 w/matrix involvement only); 2 w/moderate improvement had mixed disease: 1 no response	
De Berker ²⁷	Triamcinolone acetonide (0.1 ml of 10 mg/ml × 4) after ring block w/lidocaine	19 (46 digits)	Open	Improvement in onycholysis, pitting, subungual hyperkeratosis, ridging, thickening	Onycholysis: 18/36 digits improved, 12 resolved; pitting: 9/20 digits improved, 4 resolved; hyperkeratosis: 16/16 digits improved, 4 resolved; ridging: 15/16 digits improved, 7 resolved; thickening: 10/12 digits improved, 8 resolved	
Bleeker ²⁸	Injected triamcinolone acetonide (5 mg/ml)	3 (treated w/ needle-less-injector and syringe and needle) + 6 more pts	Open	Observed Improvement	In 3 pts treated w/both: similar results; w/needle-less: 80% success rate	
Marx ²⁹	Oral methoxysalen (0.6 mg/kg) and UVA (320–300 nm) light × 2–3/wk	10	Open	Graded by 25% increment improvement in psoriatic nail features	Onycholysis, proximal nailfold, oil drop, crumbling improved; pitting did not improve	

CsA: cyclosporine; c/w: compared with; mo: month; Obs: observation; RCT: double-blind randomized study; w/: with; wk: week; pt: patient; recur: recurrence.

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