

ORIGINAL ARTICLE

Nail psoriasis: a retrospective study on the effectiveness of systemic treatments (classical and biological therapy)

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Abstract

Background Nail psoriasis represents a challenge for specialists. There is no comparative study of systemic treatment's effectiveness at this site. *Objective:* Evaluate the response of nail psoriasis to classical and biological therapy and to compare the effectiveness and safety of the different treatments.

Methods We performed a retrospective study of 84 patients with moderate–severe psoriasis seen at our Department between January 2006 and January 2009.

Results Psoriasis was severe in 53.4%. In 75% of cases, the fingernails were affected, and the mixed form was the most frequently subtype. The mean baseline scores on the PASI and the NAPSI were 23.12 and 14.7 respectively; the correlation between the two scores fell at weeks 12 and 24 but had risen again at week 48. The baseline NAPSI score tended to be lower in women and significantly higher in patients over 65 years of age, family history of psoriasis, severe psoriasis and nail matrix involvement. In our series, 58.3% received classical treatment (acitretin, methotrexate, cyclosporin, PUVA, NUVB, REPUVA, RENUVB) and 41.7% received biological treatment (infliximab, efalizumab, etanercept, adalimumab). Significant reductions were found ($P < 0.05$) in the mean NAPSI scores at 12, 24 and 48 weeks with all the antipsoriatic agents except NUVB; significantly greater with cyclosporine ($P < 0.01$) and biological as infliximab and adalimumab at 12 and 24 weeks (differences between treatments disappeared at 48 weeks).

Conclusion The response to treatment is slower in the nail lesions than in the skin lesions. The improvement of nail psoriasis is significant both with the classical treatments significantly higher in cyclosporin; and biological treatment (infliximab and adalimumab at 12 and 24 weeks).

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Keywords

biological therapy, nail psoriasis, systemic treatment, treatment

Conflict of interest

The authors declare that they have no conflicts of interest.

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Introduction

Nail involvement appears in between 10% and 78% of cases of psoriasis¹ and commonly in the context of skin or joint disease.^{2,3} The hands are more frequently affected than the feet, and usually several nails at once. Diagnosis is established on the basis of the clinical findings and KOH culture and staining to rule out onychomycosis, which is the main differential diagnosis.⁴

Nail psoriasis always has been a therapeutic challenge for patients and dermatologists because the nail apparatus limits the

absorption of most of the topical treatments. To aid the penetration of these topical treatments, keratolytic agents are sometimes used⁴ or nail lacquer formulations with active principles at high concentrations.^{5,6} In spite of aid, often patients do not respond and only report improvement in their nail lesions when they start systemic therapy to treat a concomitant moderate–severe skin or joint psoriasis.

Very few studies have compared the behaviour of nail lesions in patients with systemic treatment. The aim of this study was to

evaluate the response of nail psoriasis to classical and biological therapy and to compare the effectiveness of the different treatments.

Materials and methods

We designed a retrospective study using the database of psoriasis patients with nail involvement seen between January 2006 and January 2009 at the Psoriasis and Phototherapy Unit of the Sagrat Cor University Hospital in Barcelona.

Patients

Inclusion criteria were the diagnosis of moderate psoriasis (PASI score ≥ 3), severe psoriasis (PASI score ≥ 10), psoriatic arthritis and the presence of psoriasis of the nails. We excluded patients with mild forms of the disease (PASI score < 3) who had been treated only with topical drugs, patients who had received topical treatment for their nails and patients whose clinical histories did not include data on the principal variables used for evaluation in the study.

Of the 350 patients with psoriasis seen between January 2006 and January 2009, 140 were ruled out for mild psoriasis not requiring systemic treatment, 114 with moderate–severe psoriasis who had received topical treatment for their nail psoriasis, and 12 because data were missing in their clinical history. The final sample comprised 84 patients.

Treatment

All patients had been treated with one or more of the following regimens: continuous oral therapy with acitretin, continuous or intermittent therapy with oral or subcutaneous methotrexate (MTX), continuous or intermittent oral therapy with cyclosporin (CyA), intermittent therapy with PUVA, intermittent therapy with NUVB (narrow band UVB), REPUVA and RENUVB, continuous subcutaneous therapy with efalizumab (EFA), intermittent and continuous subcutaneous therapy etanercept (ETA), continuous intravenous therapy with infliximab (IFX) or continuous subcutaneous adalimumab (ADA) therapy.

Evaluations

Data regarding the diagnosis of psoriasis, nail psoriasis and treatment were recorded. For the clinical evaluations, we recorded the scores obtained on the PASI (*Psoriasis Area Severity Index*) and the NAPSII (*Nail Psoriasis Severity Index*⁵) from the total score of all affected nails. Scores were recorded at baseline and at weeks 12, 24 and 48 of follow-up. We also recorded data from the last control performed in 2009 and we have studied onychomycosis with KOH smear and cultures in all affected nails, with or without onychomycosis clinical diagnosis.

Statistical analysis

The data from the clinical histories were analysed using the SPSS statistical package for Windows, version 15.0.

Data referring to the characteristics of the sample were studied using descriptive statistics. The relationships between the NAPSII

baseline score and some of the patients' characteristics were studied using the Mann–Whitney *U* and Kruskal–Wallis tests.

To study the effectiveness, we created a series of groups for comparison: type of systemic treatment, classical vs. biological; administration schedule, classical continuous vs classical intermittent; and the treatment group, that is, each specific therapy.

The effectiveness of the treatments was evaluated as the absolute and percentage decreases in the NAPSII and PASI scores from the baseline until the evaluations at 12, 24 and 48 weeks. We also calculated the percentage of patients who responded to treatment, defining response as a reduction of 75% or more of their baseline PASI score (PASI75).

The percentage of reduction in NAPSII in the treatment groups was assessed using comparisons of means tests (one-factor ANOVA) and the Mann–Whitney *U*-tests. The response rates to anti-psoriasis treatment (PASI75) between groups were compared using chi-squared tests. The relationship between the evolution of psoriasis overall and psoriasis of the nails was studied using Spearman correlation tests of the PASI and NAPSII scores.

For all tests, the level of significance was set at $P < 0.05$.

Results

Characteristics of the sample

Of the 84 patients (44 men and 40 women), psoriasis was moderate in 27.4%, severe in 53.6% and arthropathic in 19%. In most patients ($n = 63$; 75%), only the fingernails were affected and the other 25% presented involvement of both fingernails and toenails. The matrix was affected in 25%, the nail bed in 35.7%, and 39.3% presented mixed involvement. The mean score [95%CI] of psoriasis severity (PASI) was 23.12 [20.36–25.89]. The NAPSII score (assessing nail severity) tended to be lower in women and was significantly higher in patients over the age of 65 years. Other factors that were significantly correlated with the baseline NAPSII score were family history of psoriasis, degree of psoriasis (moderate $<$ arthropathic $<$ severe), the number of previous treatments and type of involvement (bed $<$ mixed $<$ matrix) (Table 1).

In all, 58.3% received classical treatment (acitretin, MTX, CyA, PUVA, NUVB, REPUVA or RENUVB) and 41.7% biological (treatment EFA, ETA, IFX or ADA) (Table 2). In 79.8% of cases, systemic therapy was associated with topical treatment for skin lesions but not for the nails. The duration of treatment ranged from 20 to 192 weeks.

Fifteen patients (17.9%) presented onychomycosis concomitantly with nail psoriasis, 76.9% in the fingernails and 23.1% in the toenails. In 10 cases, the onychomycosis had been present prior to the start of treatment and in four cases it appeared during treatment. The microorganisms isolated were *Candida albicans* ($n = 3$), *Candida parapsilosis* ($n = 3$), *Epidermophyton floccosum* ($n = 3$), *Trichophyton rubrum* ($n = 2$), *Trichophyton mentagrophytes* ($n = 2$), *Aspergillus* species ($n = 1$) and *Penicillium* species ($n = 1$).

Table 1 Severity of nail psoriasis (mean NAPS I baseline score) as a function of various factors

Various factors	Mean baseline NAPS I		
	<i>n</i>	Score [95% CI]	<i>P</i> *
Age			
<65 years	69	15.8 [13.7–18.0]	<i>P</i> = 0.010
>65 years	15	9.6 [7.3–11.9]	
Gender			
Male	44	16.2 [13.4–19.1]	<i>P</i> = 0.095
Female	40	13.0 [10.6–15.4]	
Degree of psoriasis			
Moderate	23	8.4 [6.1–10.8]	<i>P</i> < 0.0001
Severe	45	18.3 [15.8–20.8]	
Arthropathic	16	13.5 [9.4–17.6]	
Family history			
Yes	39	17.5 [14.5–20.4]	<i>P</i> = 0.005
No	45	12.3 [10.1–14.5]	
Hospitalization for psoriasis			
Yes	20	18.2 [13.3–23.0]	<i>P</i> = 0.086
No	64	13.6 [11.7–15.6]	
Site of nail involvement			
Matrix	21	18.3 [13.8–22.8]	<i>P</i> = 0.007
Bed	30	10.5 [8.8–12.1]	
Mixed	33	16.2 [13.0–19.5]	
No. previous treatments			
0	7	9.6 [4.0–15.1]	<i>P</i> = 0.017
1	28	13.0 [10.3–15.7]	
2–3	34	14.4 [11.5–17.3]	
>3	15	21.0 [15.4–26.6]	

*Statistical significance. Non-parametric test for independent samples: Mann–Whitney *U*-test for 2 categories and Kruskal–Wallis for >2 categories.

Evolution of nail psoriasis

Nail psoriasis improved in all patients. The NAPS I score fell significantly in all tests ($P < 0.001$), with classical treatments (from 12.7 to 9.7; to 6.0 and to 4.2) and with biological treatments (from 17.5 to 11.2; to 4.7 and to 1.9). Nonetheless, the percentage of change in the NAPS I score was significantly higher ($P < 0.001$) with biological treatments at 12, 24 and 48 weeks (Table 3). No significant differences were found regarding the association of topical treatment for the skin lesions either in the classical treatment group or in the biological treatment group.

All the antipsoriatic agents obtained a significant reduction ($P < 0.05$) in the mean NAPS I score at 12, 24 and 48 weeks, except NUVB (Figs 1 and 2). In classical treatment group, the reduction was significantly higher in the patients treated with CyA ($P < 0.01$) than in those treated with acitretin, MTX, PUVA, NUVB and RENUVB. In the biological treatment group, although the percentage of reduction in the NAPS I score was significantly greater with IFX and ADA at 12 and 24 weeks, the differences between biological treatments disappeared at 48 weeks (Table 3).

No significant differences were observed in the percentage of change with regard to the type of nail involvement in any of the classical and biological treatment groups, except at 48 weeks in the group treated with NUVB (Table 4).

Evolution of skin psoriasis

The rate of response to treatment of the cutaneous disease (PASI75) was 9.5% at 12 weeks, 64.3% at 24 weeks and 77.4% at 48 weeks. The percentage of patients reaching PASI75 was significantly higher with biological treatment than with classical treatment at 12 weeks (22.9% vs. 0%), at 24 weeks (80% vs. 53.1%) and at 48 weeks (94.3% vs. 65.3%).

Only 87.5% of patients treated with IFX and 12.5% treated with ADA achieving PASI75 at 12 weeks. At 24 weeks, all the groups, except the one treated with acitretin, presented cases with reduction of PASI $\geq 75\%$, ranging from 22.2% in the MTX group to 100% in the IFX, ADA and REPUVA groups. At 48 weeks, 100% of cases treated with IFX, ADA, REPUVA, CyA, NUVB and ETA reaching PASI75 (Table 5).

Relationship between NAPS I and PASI scores

The severity of the cutaneous psoriasis (the mean PASI score) also fell significantly over the visits (from 23.1 to 11.6 at 12 weeks; 4.6 at 24 weeks and 2.8 at 48 weeks; $P < 0.001$). Nonetheless, the two scores did not evolve in parallel and although they presented a positive, significant correlation at each assessment, the strong correlation observed at the baseline assessment ($r = 0.812$; $P < 0.001$), had fallen at 12 weeks ($r = 0.589$; $P < 0.001$) and 24 weeks ($r = 0.474$; $P < 0.001$), rising again at 48 weeks ($r = 0.502$; $P < 0.001$) (Fig. 3).

Later stages of follow-up

In the follow-up visit performed in the last year, 53.6% of patients continued with the same treatment, whereas 46.4% had changed or finished treatment due to: completion of the cycle ($n = 16$), efalizumab withdrawn from the market by the European Medicines Agency (EMA) in February 2009 ($n = 7$), lack of effectiveness ($n = 6$), side-effects ($n = 4$), lack of compliance ($n = 3$) or on their own initiative ($n = 2$).

Twelve patients (14.3%) suffered recrudescence or relapses of psoriasis after a period of 2–3 months. All these patients had been treated with EFA (75%) or CyA (25%).

Side-effects in the nails were found in 22 patients, including all those treated with REPUVA and RENUVB and 43% of those treated with acitretin. The side-effects were thinning of the nail plate ($n = 12$), pain ($n = 8$), paronychia ($n = 8$), pyogenic granulomas ($n = 5$), pigmentation ($n = 2$), bacterial infection ($n = 3$) and mycotic infection ($n = 4$).

Discussion

This study is a retrospective review of patients with nail psoriasis who received systemic treatment for moderate–severe psoriasis or

Table 2 Baseline NAPS and PASI scores and type of treatment

	Total (n = 84)	Classical (n = 49)	Biological (n = 35)	P*
Mean baseline NAPSI score [95% CI]	14.7 [12.8–16.6]	12.7 [10.6–14.7]	17.5 [14.2–20.9]	0.016
Mean baseline PASI score [95% CI]	23.1 [20.4–25.9]	18.8 [16.0–21.6]	29.2 [24.4–34.0]	<0.001
Treatments, n (%)				
Acitretin (oral) Initial: 25 mg/day for 6–12 weeks Maintenance: 25 mg 2–4 times/week	7/84 (8.3)	7/49 (14.3)	–	–
MTX (oral or subcutaneous) Trial dose first week 5 mg Maintenance: 7.5–25 mg	9/84 (10.7)	9/49 (18.4)	–	–
CyA (oral) Dose: 3 mg/kg/day	9/84 (10.7)	9/49 (18.4)	–	–
PUVA (intermittent) 8-MOP 0.6 mg/kg 2 h before UVA exposure	7/84 (8.3)	7/49 (14.3)	–	–
NUVB (intermittent) Narrow-band UVB	6/84 (7.1)	6/49 (12.2)	–	–
REPUVA Continuous acitretin combined intermittent PUVA	5/84 (6.0)	5/49 (10.2)	–	–
RENUVB Continuous acitretin combined intermittent RENUVB	6/84 (7.1)	6/49 (12.2)	–	–
IFX (intravenous) Dose: 5 mg/kg	8/84 (9.5)	–	8/35 (22.9)	–
ETA (subcutaneous) Initial: 50 mg two times/week for 3 months	9/84 (10.7)	–	9/35 (25.7)	–
EFA (subcutaneous) Dose: 1 mg/kg	10/84 (11.9)	–	10/35 (28.6)	–
ADA (subcutaneous) Dose: 40 mg (two injections in the first week, one injection in the second week and then one injection every 15 days)	8/84 (9.5)	–	8/35 (22.9)	–

*Statistical significance. Comparisons between classical and biological treatments. Means comparison test: one-factor ANOVA. [Correction added on 21 March 2011, after first online publication: {IFX (subcutaneous) Dose: 1 mg/kg} was changed to {IFX (intravenous) Dose 5 mg/kg}].

psoriatic arthritis. Systemic therapy is rarely prescribed for isolated nail psoriasis, but it is indicated when the condition presents concomitantly with severe skin disease, is resistant to topical treatments, substantially affects patients' quality of life, or is accompanied by pain and a significant loss of function.⁶

There are few studies of the response of nail psoriasis to systemic treatments by which the response is based on researchers' subjective evaluations of the improvement. In our study, we used the NAPS index, which not only provides an objective evaluation of the severity of nail psoriasis, but helps to evaluate response to treatment¹ and to make comparisons between therapies.

The main limitation of our study is its retrospective nature. In prospective studies, a 'washout' period is always included before the start of therapy. In our case, before initiating systemic therapy, most patients had already begun other antipsoriasis treatments and had abandoned them probably due to lack of response. Another limitation of our study was sample size. According to

type of treatment, we created small groups of between 5 and 10 patients – large enough to explore the possible differences between treatments but insufficient to obtain conclusive results.

We found nail psoriasis more frequently in patients with severe and moderate psoriasis than with the arthropathic form. The mixed subtype was the most frequently observed form. We also found a significant relationship between the severity of the nail involvement (NAPS score) and factors such as age >65 years, family history of psoriasis, type of psoriasis, the number of previous treatments and the type of nail involvement.

The results indicate that all the classical and biological systemic treatments progressively and significantly reduce the severity of nail psoriasis, with the exception of NUVB. The classical treatments used are standard antipsoriatic treatments with known effectiveness against nail involvement. Acitretin is a first-choice systemic retinoid in pustular psoriasis⁷ able to reduce subungual hyperkeratosis and improve symptoms in severe cases with multiple nail involvement.⁸ In this study, the results with acitretin were

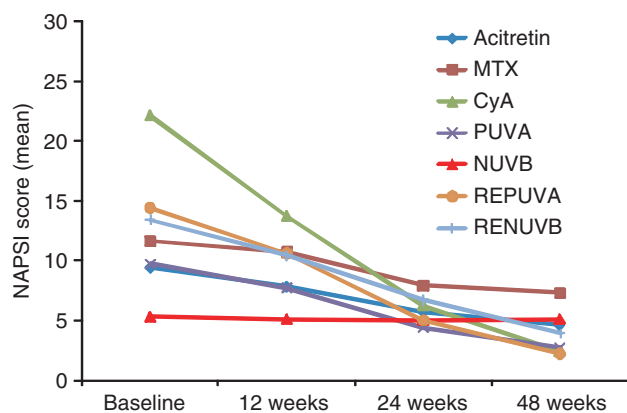
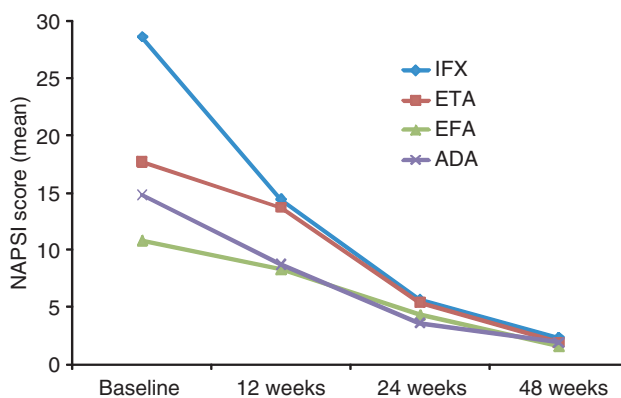
Table 3 Percentage of change in NAPSI score according to type of treatment

Treatment group	12 weeks		24 weeks		48 weeks	
	Mean percentage of change [95% CI]	P*	Mean percentage of change [95% CI]	P*	Mean percentage of change [95% CI]	P*
Classical (n = 49)	19.7 [15.4–24.1]	<0.001	45.0 [38.0–51.9]	<0.001	57.2 [48.3–66.0]	<0.001
Biological (n = 35)	32.5 [27.0–37.9]		68.6 [63.4–73.8]		86.0 [82.2–89.8]	
Treatment schedule						
Continuous classical (n = 20)	15.6 [10.9–20.2]	0.127	42.9 [33.2–52.6]	0.569	52.3 [38.9–65.8]	0.376
Intermittent classical (n = 29)	22.6 [16.0–29.2]		46.4 [36.3–56.6]		60.5 [48.2–72.7]	
Classical antipsoriatic agents						
CyA (n = 7)	37.9 [23.0–52.9]	–	71.8 [63.7–79.9]	–	89.1 [85.3–92.9]	–
Acitretin (n = 9)	18.5 [11.3–25.6]	0.005 (1)	40.5 [30.6–50.4]	<0.001 (1)	51.7 [26.7–76.7]	<0.001 (1)
MTX (n = 9)	7.3 [3.8–10.8]	<0.001 (1)	30.8 [17.2–44.3]	<0.001 (1)	34.9 [21.9–48.0]	<0.001 (1)
PUVA (n = 7)	21.4 [14.8–28]	0.055 (1)	51.4 [35.2–67.6]	0.012 (1)	69.1 [55.5–82.7]	0.023 (1)
NUVB (n = 6)	4.0 [0.5–7.4]	<0.001 (1)	3.8 [–2.1–9.8]	<0.001 (1)	5.0 [–6.9–16.8]	<0.001 (1)
REPUVA (n = 5)	26.6 [14.2–39]	0.438 (1)	65.0 [50.4–79.5]	0.364 (1)	84.6 [76.2–92.9]	0.190 (1)
RENUVB (n = 6)	20.7 [11.1–30.4]	0.026 (1)	48.2 [36.1–60.4]	<0.001 (1)	64.4 [47.3–81.5]	0.003 (1)
Biological antipsoriatic agents						
IFX (n = 8)	50.1 [38.7–61.4]	–	80.6 [73.2–88]	–	91.5 [86.5–96.5]	–
ETA (n = 9)	24.3 [16.1–32.4]	0.001 (2)	68.2 [60.7–75.7]	0.015 (2)	86.7 [77.8–95.6]	0.423 (2)
EFA (n = 10)	22.4 [17.1–27.7]	<0.001 (2)	55.7 [43.1–68.3]	0.006 (2)	82.5 [72.8–92.1]	0.237 (2)
ADA (n = 8)	36.6 [24.2–49]	0.105 (2)	73.1 [64.7–81.4]	0.083 (2)	84.2 [75.6–92.7]	0.083 (2)

*Statistical significance. Non-parametric test for independent samples: Mann–Whitney U.

(1) Comparison of classical antipsoriatics vs. CyA.

(2) Comparison of biological antipsoriatics vs. IFX.

**Figure 1** Evolution NAPSI scores with classic treatments.**Figure 2** Evolution NAPSI scores with biological treatments.

comparable to those published by Tosti *et al.*, who reported a 41% reduction in the NAPSI score at 6 months, a figure similar to the 40.5% observed in our study at 24 weeks.⁹

Similar levels of effectiveness were obtained with methotrexate. Although we found only one reference to treatment with MTX,¹⁰ most professionals agree that it may be beneficial^{2,4} and may improve nail lesions in parallel to skin lesions.

Cyclosporin was the most effective classical systemic treatment. We reported its capacity to improve nail psoriasis several years ago in a series of 70 psoriatic patients who, after oral treatment with CyA, presented long-term improvements in the lesions of the matrix and the bed.¹¹ Cyclosporin's superiority over systemic retinoids was also demonstrated by Mahrle *et al.* in a randomized trial with 210 patients.¹²

Table 4 Percentage of reduction in NAPSI score according to treatment group and type of nail involvement

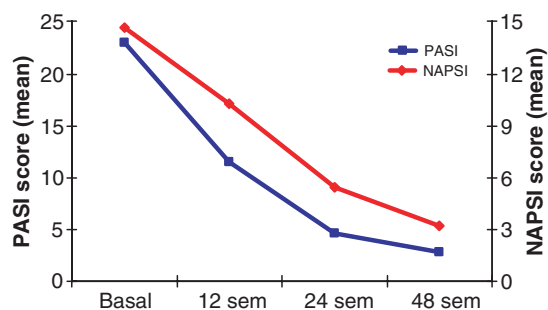
	Matrix (n = 9) Mean [95%CI]	Bed (n = 19) Mean [95%CI]	Mixed (n = 21) Mean [95%CI]	P*
Classical treatments				
12 weeks	22.3 [9.9–34.7]	18.4 [13.4–23.4]	19.9 [11.5–28.2]	0.853
24 weeks	48.4 [31.3–65.5]	42.6 [32.4–52.7]	45.7 [32.8–58.6]	0.813
48 weeks	61.9 [39.4–84.4]	53.1 [40.8–65.5]	58.8 [42.3–75.2]	0.427
Biological treatments				
12 weeks	37.6 [25.7–49.5]	27.9 [20.1–35.7]	31.5 [21.6–41.4]	0.425
24 weeks	70.1 [59.9–80.3]	64.0 [53.5–74.4]	71.3 [62.3–80.3]	0.43
48 weeks	84.4 [76.9–92.0]	85.0 [77.0–93.0]	88.5 [82.4–94.6]	0.495

*Statistical significance. Non-parametric test for independent samples: Kruskal–Wallis.

Table 5 Percentage of patients with PASI score reduction $\geq 75\%$ according to type of treatment

	PASI75 12 weeks n (%)	PASI75 24 weeks n (%)	PASI75 48 weeks n (%)
Classical	0/49 (0)	26/49 (53.1)	32/49 (65.3)
Acitretin	0/7 (0)	0/7 (0)	1/7 (14.3)
MTX	0/9 (0)	2/9 (22.2)	4/9 (44.4)
CyA	0/9 (0)	8/9 (88.9)	9/9 (100)
PUVA	0/7 (0)	4/7 (57.1)	3/7 (42.9)
NUVB	0/6 (0)	4/6 (66.7)	6/6 (100)
REPUVA	0/5 (0)	5/5 (100)	5/5 (100)
RENUVB	0/6 (0)	3/6 (50.0)	4/6 (66.7)
Biological	8/35 (22.9)	28/35 (80.0)	33/35 (94.3)
IFX	7/8 (87.5)	8/8 (100)	8/8 (100)
ETA	0/9 (0)	8/9 (88.9)	9/9 (100)
EFA	0/10 (0)	4/10 (40.0)	8/10 (80.0)
ADA	1/8 (12.5)	8/8 (100)	8/8 (100)
P*	<0.001	<0.01	0.001

*Statistical significance of the comparison between types of classical and biological treatments. Chi-squared test.



*Statistical significance. Spearman correlation test.
 r = Spearman's Rho correlation coefficient

Figure 3 Evolution of mean NAPS I and PASI scores. Correlation between scores.

As regards photo(chemo)therapy, treatment with PUVA improved nail psoriasis, but its effects vary according to the type of lesion.¹³ However, in our study, we did not find differences according to type of involvement (matrix, bed or mixed). No data are available on the effect of treatment with NUVB on nail psoriasis and our data suggest that it is not effective for treating nail psoriasis.

Biological treatments were the most effective approach to nail psoriasis. Infliximab is one of the most widely studied agents^{14–16} and is considered by many to be the best current treatment option for nail psoriasis.^{17,18} Response to IFX has been reported in patients with severe nail psoriasis refractory to other systemic therapies.¹⁹ In a randomized controlled study, IFX obtained fast improvement of nail symptoms within a few weeks and maintained its effect over a period of months.¹⁴ In our study, IFX acted faster than EFA and ETA, although at weeks 24 and 48, the rest of the biological treatments reached the same levels.

The data available on efalizumab, before its withdrawal from circulation, indicated its effectiveness for treating nail psoriasis.²⁰ In a multicentre study with 1266 patients, over 20% of those presenting psoriasis of the nails improved by 50% or more after 12 weeks of treatment with EFA.²¹ In our study, in contrast, the mean NAPS I score did not fall by more than 50% until week 24.

Etanercept also proved effective for reducing nail psoriasis in our study. In one post-hoc analysis of over 700 cases treated with ETA, patients' nail symptoms improved by 51% after 54 weeks of treatment.²² In another retrospective study of 66 patients treated with ETA, all patients presented a significant improvement in nail disease after the first and second cycles of treatment.²³ A rapid improvement has also been reported with ETA in a patient who had been refractory to other treatments.²⁴

Adalimumab is one of the most recently authorized biological treatments for psoriasis, as is ustekinumab (approved in 2009). Few data are available on ADA's effectiveness in treating nail psoriasis. In a recent study in patients with psoriatic arthritis, treatment with ADA was able to reduce the NAPS I score at 12 weeks by 44%.²⁵ In another study of 21 patients, treatment

with ADA also achieved a significant improvement in the NAPSI at 12 and 24 weeks.²⁶ Our results also support the effectiveness of ADA for treating psoriasis of the nails.

Interestingly, although patients who received biological treatments presented greater initial severity of both cutaneous and nail psoriasis than those treated with classical treatments, at week 48 the situation had reversed. [Correction added on 21 March 2011, after first online publication: (classical treatments presented greater initial severity of both cutaneous and nail psoriasis than those treated with biological treatments) was changed to (biological treatments presented greater initial severity of both cutaneous and nail psoriasis than those treated with classical treatments)].

The relationship between the evolution of the NAPSI and PASI scores also deserves comment. As the cutaneous lesions improved, the nail lesions improved as well; however, the correlation between the two fell at weeks 12 and 24, before rising again at week 48. This finding may suggest a slower response in nail lesions than in skin lesions, probably due to their slower rate of growth.

Another interesting finding was the fact that the evolution of the nail lesions did not depend on the type of involvement (matrix, bed or mixed) in any of the treatment groups, in contrast to certain topical treatments⁶ and photo(chemo)therapy.¹⁵

Only patients who had received treatment regimens including acitretin or phototherapy (REPUVA and RENUVB) presented side-effects in the nails. It is known that many of the side-effects of acitretin occur at this site, for instance onycholysis, intense brittleness and pyogenic granulomas.⁴

Studies published in recent years have suggested a higher prevalence of onychomycosis in patients with nail psoriasis,²⁷ reaching 30% in previous work by our own group.²⁸ This suggests that KOH and mycological cultures should be performed before and during treatment of nail psoriasis. In our group of patients, we observed 15 cases (17.9%) of onychomycosis concomitant with psoriasis. Interestingly, most were patients who had not received treatment for their nail lesions. Once again, the prevalence of onychomycosis was clearly higher than that expected in the normal population – 2.6% in Spain²⁹ and 6.48% in Canada³⁰ – and we stress that most cases were observed in patients with psoriasis of the nails prior to treatment, the species observed being dermatophytes, yeasts and moulds.

In spite of the limitations of the study (mainly related to its retrospective nature), the following conclusions can be drawn.

1. The PASI and NAPSI scores indicate a clear correlation between the clinical activity of the skin and nail psoriasis. However, the results suggest that the response to treatment may be slower in the nail lesions than in the skin lesions.
2. The NAPSI score tended to be lower in women and higher in patients over 65 years, those with psoriasis of the nail matrix, with severe psoriasis, with family history of psoriasis, with a greater number of previous systemic treatments.
3. The nail psoriasis improvement was significant both with the classical treatments (with the exception of NUVB) and

with biological treatments. Nonetheless, the percentage of change in the NAPSI score was significantly greater with biological treatments.

4. The percentages of change with the classical treatments were significantly higher in the patients treated with CyA than in patients treated with acitretin, MTX, PUVA, NUVB and RENUVB.
5. With the biological treatments, although the percentage of reduction in the NAPSI score was significantly greater with IFX and ADA at 12 and 24 weeks, the differences between treatments disappeared at 48 weeks.
6. No significant differences were observed with regard to the percentage of change depending on the type of nail involvement (matrix, bed or mixed) in any of the classical or biological treatment groups.
7. Eighteen per cent of patients presented some type of onychomycosis in association with nail psoriasis. Previous studies have reported similarly high figures for the coexistence of these two entities. Nail psoriasis, especially of the fingernails, should be added to the list of illnesses that predispose to onychomycosis.

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