Therapies for Dactylitis in Psoriatic Arthritis. A Systematic Review

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ABSTRACT. Dactylitis is a hallmark clinical feature of psoriatic arthritis (PsA). Acute dactylitis appears to be a severity marker for PsA and psoriasis. Traditionally, clinicians have used nonsteroidal antiinflammatory rheumatic drugs and local corticosteroid injections to treat dactylitis, although conventional disease modifying antirheumatic drugs also are recommended. In this systematic review, the limited data on treatments for dactylitis in PsA highlight the need for a valid, reliable, and responsive clinical outcome measure. Infliximab is the only drug to demonstrate significant improvement of dactylitis during a clinical study. (First Release May 15 2006; J Rheumatol 2006;33:1439–41)

Key Indexing Terms:
PSORIATIC ARTHRITIS DACTYLITIS TREATMENT SYSTEMATIC REVIEW

INTRODUCTION

Dactylitis has been defined as "uniform swelling such that the soft tissues between the metacarpophalangeal and proximal interphalangeal, proximal and distal interphalangeal, and/or distal interphalangeal joint and digital tuft are diffusely swollen to the extent that the actual joint swelling could no longer be independently recognized[1]." Dactylitis is a hallmark clinical feature in patients with spondyloarthropathies (SpA) and is commonly observed in rheumatology clinics[1].

Dactylitis occurs in 16%–48% of cases of psoriatic arthritis (PsA)[2-5]. According to some investigators, dactylitis is predominantly due to swelling and inflammation in the flexor tendon sheaths[6], although other groups have recorded joint synovitis as well as tenosynovitis[7]. Acute dactylitis has been shown to be a clinical indicator of disease severity in PsA[5]. Recurrent dactylitis, often in the same digit(s), may be the only clinical manifestation of PsA[8].

The treatment of dactylitis is empirical. Nonsteroidal antiinflammatory drugs (NSAID) are usually employed initially, but many clinicians will rapidly progress to treatment with injected corticosteroids. In resistant cases, disease modifying antirheumatic drugs (DMARD) are used; however, this is nearly always in the context of coexisting active disease.

The intent of this review is to identify and evaluate the efficacy data of therapies used to treat dactylitis in patients with PsA.

Search Strategy

The evidence in this review was compiled following a search of Ovid Medline dating from 1966 to the present. Several articles were identified using the following search terms: "dactylitis" (as key search word, 172 articles) and "psoriatic arthritis" (treatment only, 532 articles). Crossing these terms and applying the inclusion and exclusion criteria outlined below, 12 articles were selected for this review of dactylitis. Manual searching was performed on reference lists of trials selected through the electronic search and from the author's own files.

Inclusion criterion: Therapeutic trials of PsA; within this group, those studies in which dactylitis was assessed as a separate outcome measure were identified.

Exclusion criterion: Studies of dactylitis in patients without psoriatic arthritis were excluded.

Outcome Measures

Regrettably, there are no validated instruments with which to assess the presence or severity of dactylitis. Some studies used a simple count of dactylitic digits (the presence of dactylitis based on clinician opinion). In one study, dactylitis was graded from 1 to 4 (mild to severe)[9]. In others, the severity was graded 0–3 and all 20 digits were counted[10,11].

RESULTS

Studies using dactylitis as an outcome measure were few in number. Where dactylitis was assessed, only 2 studies of nonbiologic drugs and 3 of biologic drugs were found. No studies of local steroid injections or of NSAID were identified.

Nonbiologic drugs used in the treatment of dactylitis are displayed in Table 1. The data are summarized below.

Sulfasalazine. In the Department of Veterans Affairs Study, Clegg, *et al*[12] found an insignificant difference between placebo and sulfasalazine (SSZ) after 36 weeks of treatment. Investigators used a simple count of dactylitic digits as the outcome measure, but the absolute numbers and differences from baseline to endpoint were small. Mean baseline dactylitis involvement was 3.8 digits for SSZ and 2.6 digits for placebo. At 36 weeks, change from baseline was –0.5 ± 4.2 for SSZ and 0.9 ± 4.1 for placebo.

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Table 1. Summary of trials of nonbiologic disease modifying drugs used in psoriatic arthritis: effect on dactylitis.

Agent	Study	No. of Patients	Study Type	Outcome Measure	Results	p	Effect Size	Comments
Sulfasalazine	Clegg[12]	221	DB, RPC	Simple count of digits	Change at 36 weeks: SSZ –0.5 ± 4.2 Pbo –0.9 ± 4.1	0.43	0.20	
Leflunomide	Kaltwasser[9]	186	DB,RPC	Dactylitis scored 1 to 4*	Changes at 24 weeks: LEF –0.9 ± 2.7 Pbo –0.2 ± 2.4	0.2	0.33	* Data courtesy of P. Nash (not included in publication)
Cyclosporine, sulfasalazine, symptomatic therapy	Salvarani[13]	99	OL	No. of dactylitic digits	Only 4 subjects developed dactylitis (2 CsA, 1 SSZ, 1 symptomatic therapy)	N/A	N/A	Not enough data to make meaningful comparison

CsA: cyclosporine; LEF: leflunomide; N/A: not applicable; OL: open label; Pbo: placebo; RPC: randomized, placebo-controlled; SSZ: sulfasalazine.

Leflunomide (LEF). In TOPAS (Treatment of Psoriatic Arthritis Study), Kaltwasser, *et al*[9] graded dactylitis from 1 to 4 (where 4 was most severe) and found an insignificant difference between placebo and LEF. At 24 weeks, the change from baseline was –0.9 ± 2.7 for LEF and –0.2 ± 2.4 for placebo. These data were not included in the published results, but were provided courtesy of Dr. Peter Nash.

Cyclosporine (CsA) and sulfasalazine. Salvarani, *et al*[13] compared treatment with CsA, SSZ, and symptomatic therapy (ST) in patients with PsA using a simple count of patients developing dactylitis as the outcome measure. Very few patients developed dactylitis during the course of the study (2 CsA, 1 SSZ, 1 ST); thus, no conclusions could be drawn.

Biologic drugs used in the treatment of dactylitis are displayed in Table 2. The data are summarized below.

Etanercept. Dactylitis was not part of the assessment profile in controlled studies with etanercept[14,15].

Infliximab. Both the IMPACT 1[10] and IMPACT 2[16] trials assessed dactylitis in response to treatment with infliximab. In IMPACT 1, a nonvalidated dactylitis instrument was used in which all 20 digits were assessed and graded from 0 to 3 (see Table 2). A significant difference in dactylitis change scores was found (change at 16 weeks: 1.94 ± 0.23 for infliximab, and 0.58 ± 0.20 for placebo). However, mean baseline dactylitis scores (infliximab 2.3, placebo 2.0) were low for both groups; thus, there was little scope for change. Further, the mean improvement is equivalent to one digit improving by 1 point on the 0–3 severity scale; therefore, the effect size was correspondingly small. The absolute numbers of patients with dactylitis at baseline were not provided.

For IMPACT 2, the method of assessing dactylitis was changed to the percentage of patients with dactylitis, but the results were similar: a significant benefit in favor of infliximab[16]. The absolute numbers of patients who improved were estimated from data provided in the publication (numbers of patients changing from having dactylitis to not having dactylitis at 14 weeks: infliximab, 23 patients; placebo, 13 patients).

Table 2. Summary of trials of biologic drugs used in psoriatic arthritis: effect on dactylitis.

Agent	Study	No. of Patients	Study Type	Outcome Measure	Results	p	Effect Size	Comments
Infliximab	Salvarani[30]	16	OL	No. of dactylitic digits	No dactylitis observed during the study period	NA	NA	INX added to MTX
Infliximab	Antoni[10] (IMPACT 1)	104	DB, RPC	Dactylitis score*	Change at 16 weeks: INX –1.94 ± 0.23 Pbo –0.58 ± 0.20	< 0.001	0.41	Effect size estimated from data provided in the publication
Infliximab	Antoni[16] (IMPACT 2)	200	DB, RPC	Percentage of patients with dactylitis of hands/feet	Change at 14 weeks: INX –23 patients Pbo –13 patients	0.025	NA	Estimated from data provided in the publication
Adalimumab	Mease[11]	249	DB, RPC	Dactylitis score*	Results not given: no statistical difference at 24 wks	NA	NA	NA

DB: double-blind; INX: infliximab; NA: not applicable; OL: open label; Pbo: placebo; RPC: randomized, placebo-controlled; MTX: methotrexate. * All 20 digits were examined. Dactylitis was identified *only* if the entire digit was involved (e.g., not if there was prominent periarticular swelling about the PIP that did not extend to the whole digit). Dactylitis was graded on a scale of 0–3, where 1 was definite dactylitis, 2 moderate, and 3 the most severe form with prominent inflammation. Summed score was used (range 0–60). The following trials were not included as dactylitis was not part of the assessment schedule: Mease, *et al*, 2000[14], Mease, *et al*, 2004[15].

Adalimumab. In a 24-week, double-blind, randomized, placebo-controlled trial of adalimumab in patients with moderate to severe active PsA, the outcome measure used was identical to the one used by Antoni, *et al*[10] in the IMPACT I study reported above (i.e., 20 digits were graded 0–3). Specific results for dactylitis were not presented in the publication; however, they were described in the text. Adalimumab-treated patients had greater improvement than placebo patients, but the results did not reach statistical significance[11].

Treatment Recommendations

Infliximab is effective for the treatment of dactylitis in PsA (level 1b, grade B); however, dactylitis was a secondary outcome measure and improvement was modest. Due to the limited data in the other studies, no further recommendations can be made.

Conclusions and Limitations

This brief review has revealed the dearth of evidence for treating dactylitis in patients with PsA. The most commonly used therapies, NSAID and local corticosteroid injections, have not been assessed formally. Of the biologic drugs, only infliximab has proven efficacy. Anecdotally, etanercept and adalimumab also have been effective. None of the trials has used a valid assessment tool. The lack of a validated, sensitive measure for dactylitis has hampered study of this important manifestation of PsA.

Because dactylitis may represent a composite of pathological features, it could be argued that an assessment of tenderness and swelling in the component parts (proximal interphalangeal joint and distal interphalangeal joint) is sufficient. This argument, however, ignores that dactylitis, while not unique to PsA, is an essential clinical manifestation of this disease. Further development of a valid, sensitive measure to quantify dactylitis is urgently required.

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