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Title: Psoriasis flare with corticosteroid use in Psoriatic Arthritis

Running title: Psoriasis flare with corticosteroid use in Psoriatic Arthritis

LC Coates<sup>1</sup>, PS Helliwell<sup>1</sup>

Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, UK and Leeds Musculoskeletal Biomedical Research Unit, Leeds Teaching Hospitals NHS Trust, Leeds, UK.

Corresponding author

Dr Philip S Helliwell

Chapel Allerton Hospital, Chapeltown Road, Leeds, LS7 4SA

Tel - +44 113 392 3064

Fax - +44 113 392 4991

Email – [p.helliwell@leeds.ac.uk](mailto:p.helliwell@leeds.ac.uk)

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Corticosteroids are used as an adjunct to disease-modifying therapy in inflammatory arthritides. Psoriasis flares can occur with tapering of steroids, including a return of usual psoriasis, rebound flares or glucocorticoid-induced generalized pustular psoriasis.<sup>1</sup> Therefore recommendations for PsA management highlight the possible risk of psoriasis flare.<sup>2,3</sup>

Observational data have shown that steroids are commonly used in PsA<sup>4</sup> and psoriasis<sup>5,6</sup>. It seems that physicians should see psoriasis flares, however it is not commonly reported in clinical practice. Rheumatologists use both intraarticular (IA) and intramuscular (IM) steroids<sup>7</sup>. It is hoped that giving steroids IA reduces the systemic effect. However there is good evidence for systemic absorption of IA steroids<sup>8</sup>. It has been suggested that there is a higher risk of flare with prednisolone<sup>9</sup>.

We aimed to identify the incidence of psoriasis flare following IA and IM steroids in patients with PsA.

## Methods

A total of 206 adults with recent onset PsA, naïve to treatment, were recruited into the Tight Control of Psoriatic Arthritis (TICOPA) trial<sup>10</sup>. Patients in either arm could receive IA or IM steroids. The psoriasis activity and severity index (PASI) was recorded every four weeks in the tight control arm and every 12 weeks in the standard care arm. Pre and post administration PASIs were compared using the Wilcoxon signed rank test. Any related adverse events (AEs) were identified.

## Results

Of 206 patients, the majority (84.5%, n=174) had active psoriasis, but the median PASI score was 2.6 (IQR: 1.2, 4.8).

A total of 307 injections were given. Selecting for psoriasis identified 161 episodes of steroid use in 101 patients. There were 50 IA injections (median dose 40mg methylprednisolone, range 5-120mg) and 111 IM injections (median dose 120mg, range 40-160mg). Steroid use was equal in the two trial arms (tight control n=76, standard care n=85).

Pre-administration PASI scores were all available. PASI at follow up was missing in 41 cases leaving 120 episodes. The baseline median PASI was 1.8 (IQ range 0.65, 3.8) with median change 0.0 (IQ range -1.18, 0.50, ns). The majority of patients (74/120, 61.7%) showed no increase in PASI. However 36 (30.0%) showed an increase in PASI of 0.1-2 and 10 had an increase of  $\geq 2$ . Nine had follow up 12 weeks later.

Overall, there was no significant change in PASI regardless of route, type or dose of steroid administered (figure 1). Of those with increase in PASI of  $\geq 2$  (n=10), nine received 120mg dexamethasone IM (table 1).

There were no flares of psoriasis recorded as AEs temporally related to steroids. The majority of patients were taking DMARDs (126/149 episodes) with most on methotrexate (alone 90/149, in combination 30/149).

## Discussion

This analysis found no evidence for an overall change in psoriasis related to steroid use in PsA but did identify 10 patients with PASI increase  $\geq 2$ . Those experiencing this “flare” mostly received higher dose IM prednisolone. None were reported as adverse events. The reasons for this are unclear but suggest a disconnect between PASI scores and perceived flare. In nine cases there was a 12 week gap between assessments and other factors may have contributed.

We recognize that PASI may not be the best measure for psoriasis flare but no recognized definition exists. In mild psoriasis, PASI may not accurately reflect disease activity and within a PASI score, a change in psoriasis distribution or phenotype could occur.

The baseline psoriasis activity was mild, in contrast to dermatology cohorts. The risk of flare with corticosteroids in those with severe skin disease may differ. Likewise the majority of these patients were also taking concomitant methotrexate, which may impact on their risk of a psoriasis flare.

Steroids are useful in patients with PsA for rapid anti-inflammatory effect. If they are used for the minimal time and with DMARDs then we hope the associated risks can be minimized. It seems that the risk of psoriasis flare is around 8% particularly with higher dosage IM administration and patients should be counselled about this.

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Table 1 – PASI and steroid administered to patients with increase in PASI>2

Patient	Randomisation	Baseline PASI	Next PASI	Time between PASIs (weeks)	Change in PASI score	Steroid given	Dose	Route	Concomitant DMARD	Number of injection causing flare/total number of injections in study
1	StdC	0.9	3	12	2.1	Depomedrone	120mg	IM	MTX	2/2
2	TC	0.3	3	4	2.7	Depomedrone	120mg	IM	none	1/1
3	StdC	2.6	6.0	12	3.4	Depomedrone	120mg	IM	MTX	1/1
4	StdC	1.0	4.4	12	3.4	Depomedrone	120mg	IM	none	1/1
5	StdC	0.4	4.0	12	3.6	Depomedrone	120mg	IM	MTX	1/2
6	TC	4.8	10.4	12	5.6	Depomedrone	120mg	IM	MTX	1/4
7	TC	7.5	13.2	12	5.7	Depomedrone	120mg	IM	MTX	1/1
8	StdC	7.2	14.4	12	7.2	Depomedrone	120mg	IM	MTX	2/3
9	StdC	8.2	26.7	12	18.5	Depomedrone	120mg	IM	MTX	1/1
10	StdC	8.6	30.8	12	22.2	Depomedrone	80mg	IA	MTX and SSZ	1/1

IA – intraarticular, IM – intramuscular, MTX – methotrexate, PASI – psoriasis area and severity index, SSZ – sulfasalazine, StdC – standard care arm, TC – tight control arm

Figure 1 – Change in PASI score by (a) route, (b) type and (c) dose of corticosteroid administered.

