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Glucocorticoid use in psoriatic arthritis and treatment outcomes: does the gender have a role?

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Abstract

Background Systemic glucocorticoids are commonly used in practice in the treatment of psoriatic arthritis. However, authorities advise against prescribing it, primarily because of the risk of psoriasis flare-ups. The authors aimed to assess the glucocorticoid use in psoriatic arthritis (PsA), factors associated with the use of glucocorticoids and to uncover whether gender has an impact on glucocorticoid use and treatment responses. Disease-modifying antirheumatic drug (DMARD)-naive PsA patients were included in this cross-sectional study. Baseline clinical and demographic characteristics were recorded. After starting DMARD treatment, patients were followed for 2 years. The number of patients who started glucocorticoids, the clinical demographics of these patients, the duration of glucocorticoid administration, and the dose for administration were recorded. Patient outcomes and gender differences were analyzed. Disease activity was measured using the Disease Activity Scale 28 (DAS28-CRP) and the Disease Activity Index for Psoriatic Arthritis (DAPSA).

Results Fifty-five of the 141 patients (39%) received glucocorticoids at the 2-year follow-up. There was no difference between the sexes who are in remission-low disease activity (LDA) on cDMARD monotherapy ($p = 0.300$). Glucocorticoid usage ($p = 0.660$), dose ($p = 0.054$), and duration ($p = 0.159$) did not differ between male and female patients. Higher glucocorticoid doses were associated with dactylitis, higher CRP levels, higher DAS-28 and DAPSA scores, and longer (> 3 months) glucocorticoid administration. Glucocorticoid duration was longer in patients with higher TJS, SJS, serum CRP, higher DAS-28 and DAPSA scores, and higher glucocorticoid doses. Sustained remission-LDA was achieved in 16 of 55 patients after cessation of glucocorticoids and no sex difference was observed.

Conclusion Systemic glucocorticoids are commonly prescribed in PsA, and when added to treatment even for short periods and in low doses, they help achieve significant disease control. Except for axial involvement, there is no difference in treatment responses between male and female patients, making it unnecessary to make a gender distinction in the treatment algorithm. Given these findings, prospective studies are needed to evaluate glucocorticoids as a bridging treatment in PsA, such as rheumatoid arthritis.

Keywords Psoriatic arthritis, Glucocorticoid, Gender, Treatment outcome

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Background

Psoriatic arthritis (PsA) is a chronic inflammatory arthritis characterized by peripheral arthritis, spondyloarthritis, enthesitis, and dactylitis. Psoriatic arthritis affects women and men equally, with a prevalence of approximately 1 to 2 per 1000 in the general population [1, 2]. Estimates suggest that the prevalence of PsA in patients with psoriasis ranges from 4 to 30% [3, 4]. Clinical

features used to assess disease severity in PsA patients include peripheral arthritis, skin and nail psoriasis, axial disease, enthesitis, and dactylitis [5, 6].

Methotrexate is the first-line disease-modifying anti-inflammatory drug (DMARD) used to control peripheral arthritis in PsA. Recently, leflunomide and sulphasalazine have also taken place in the EULAR and GRAPPA treatment guidelines [7, 8]. Although recent studies have focused on biological DMARDs in patients who have not responded to methotrexate, there are many patients whose disease activity can be controlled by the addition of glucocorticoids in real life. The conditional use of glucocorticoids in peripheral arthritis is recommended in the 2022 GRAPPA treatment guideline [8]. However, the dose and duration of glucocorticoids have not yet been studied in randomized controlled trials.

Another issue is that all study designs, diagnoses, and treatment guidelines were published gender-neutral until the last few years. However, differences between men and women have been found in many rheumatic diseases. The data suggest that female PsA patients are more likely to have polyarticular involvement, while males have oligoarticular and axial involvement [9]. While no gender differences were found in terms of retention rate and response to methotrexate, female patients showed a lower retention rate than their male counterparts with respect to tumor necrosis factor (TNF) inhibitors [10, 11]. Nonetheless, these differences require further consideration of gender differences in diagnosis and treatment. Aside from methotrexate and TNF inhibitors, there is also no data on whether there is a gender difference in glucocorticoid use.

The aim of this cross-sectional study is to determine the frequency of glucocorticoid use and the factors associated with glucocorticoid use in PsA patients and to determine whether there are gender differences in treatment selection and outcomes.

Methods

Study design and participants

In this cross-sectional study, patients with treatment-naive psoriatic arthritis (PsA) were enrolled between January 12, 2020 and January 12, 2022, in a rheumatology outpatient clinic. All patients were over 18 years of age and met the classification of psoriatic arthritis (CASPAR) criteria for PsA with the condition of peripheral arthritis [12]. Patients with concomitant rheumatic disease, malignant diseases, pregnancy, and lactation were excluded from the study. Those who had a contraindication or intolerance for DMARDs (methotrexate, sulphasalazine, leflunomide) or glucocorticoids were excluded from the study. NSAIDs were allowed during the study. Concomitant medications had to be stable for ≥ 3 months. Patients who had glucocorticoid treatment indications other than peripheral arthritis treatment and were started on medication were excluded from the study.

Procedures

Treatment naive PsA patients were followed for 2 years after starting DMARD treatment. The number of patients who started glucocorticoids, the clinical demographics of these patients, and the duration and dose of glucocorticoid administration were recorded. The duration of glucocorticoid administration was analyzed into two categories; < 3 months and 3 months. The administered dose was evaluated in 3 levels < 7.5 mg (low prednisolone dose), 7.5–30 mg (medium dose), and 30 mg (high dose). Patient outcomes and gender differences were analyzed. Before drug cessation, a glucocorticoid tapering regimen was used according to the treatment dose. The tapering regimen was applied as follows;

- If prednisone dose ≥ 30 mg/day, reduce 5 mg/day every week.

-If the prednisone dose is 7.5 mg–30 mg/day, a reduction of 2.5 mg/day every week.

-If the prednisone dose is ≤ 7.5 mg/day, reduce it to 1 mg/day every week.

Patient outcomes and gender differences were analyzed.

Disease activity was measured by the Disease Activity Scale 28 (DAS28-CRP) [13] and Disease Activity Index for Psoriatic Arthritis (DAPSA) [14]. Definitions used for remission/low disease activity (LDA) were DAS-28 (cut-off for remission < 2.6 and LDA ≤ 3.2 and/or DAPSA (cut-off for remission < 5 and LDA ≤ 14).

Patients who were intolerant or who had inadequate response to cDMARDs were started on TNF inhibitor therapy (infliximab, adalimumab, etanercept, golimumab, certolizumab pegol) in accordance with EULAR and GRAPPA guidelines [7, 8].

Measures

All study patients underwent assessment by a rheumatologist which included a complete history, physical examination, and laboratory evaluation at 3-month intervals and baseline radiological assessment (radiographs of the hands, feet, sacroiliac joints (conventional anteroposterior view of the pelvis) and the cervical, thoracic and lumbar spine (lateral and anteroposterior views)). Demographic and disease characteristics included: age, gender, symptom duration of PsA, swollen joint count (SJC), tender joint count (TJC), distal interphalangeal (dıp) joint involvement, axial involvement (cervical, thoracal, and lumbar vertebrae), sacroiliitis, enthesitis, dactylitis, and type of psoriasis (plaque, pustular, psoriatic nail distrophy involvement, and others). A physical examination

was performed to assess enthesitis as measured by the Maastricht Ankylosing Spondylitis Enthesitis Score [15].

The laboratory assessments included C-reactive protein (CRP), complete blood count (CBC), blood urea nitrogen (BUN), creatinine, alanine aminotransferase (ALT), and aspartate aminotransferase (AST) every 3 months.

Written informed consent was obtained from all participants. There were no missing data.

Statistical analysis

Differences between genders in values of continuous variables were assessed by *t*-tests or Mann-Whitney tests. The association between categorical variables and gender was assessed by the Pearson chi-square test or Fisher's exact test. The significant independent variables in the univariate analyses were tested in multivariate stepwise regression models. The results were expressed as odds ratios (ORs) in logistic regression models and as regression coefficients in linear regression models. Pearson's and Spearman correlation analysis was performed to analyze the correlation between glucocorticoid dose and duration. The 95% confidence interval (95% CI) was calculated and a *P* value less than 0.05 was considered significant. Power analysis is performed with a power of 0.80.

SPSS, version 26 was used for the data analysis.

Results

Patient's characteristics

A total of 141 patients were included in the study. Ninety-six (68.1%) patients were female and 45 (31.9%) patients were male. The mean age was 49.3 ± 13.5 years. The mean duration of symptoms was 3.22 ± 6.19 years. Seventeen (12.1%) patients had distal interphalangeal joint involvement. Twelve (8.5%) patients have dactylitis. Thirty (21.3%) patients had axial disease. Twenty-three (16.3%) patients had unilateral/bilateral sacroiliitis. Psoriatic nail dystrophy was observed in 8 (5.7%) patients. Ten (7.1%) patients had no psoriatic skin lesions at presentation. The mean DAS 28 score was 3.5 ± 0.6 and the mean DAPSA score was 21.2 ± 7.2.

The data showed that male patients had more unilateral/bilateral sacroiliitis than female patients (*p*: 0.023). TNF inhibitors have been used more frequently in men than in women (p: 0.006). Analysis showed no difference in age, symptom duration, distal interphalangeal joint involvement, enthesitis, dactylitis, axial disease, psoriatic nail dystrophy, pustular psoriasis, TJS, SJS, VAS, CRP, DAS-28, and DAPSA between female and male patients. Male patients had significantly higher serum uric acid levels than female patients (*p*:0.000).

Baseline clinical differences between genders are shown in Table 1.

Fifty-three (37.5%) patients (36% of female patients and 42% of male patients) had sustained remission for 52 weeks on cDMARD monotherapy.

Glucocorticoid therapy

Fifty-five patients (39%) received glucocorticoid therapy (42 women, 13 men). Forty-seven (85%) of the patients using glucocorticoids received low-dose treatment (< 7.5 mg prednisolone), while 8 (15%) received medium-dose treatment (7.5–30 mg). There were no patients using high-dose glucocorticoids. While 47 (85%) of these patients were treated for less than 3 months, 8 of them used glucocorticoids for more than 3 months. The frequency of glucocorticoid use, dose, and duration of administration were similar in males and females ($p = 0.660$, $p = 0.054$, and $p = 0.159$). Clinical differences between genders are shown in Table 1. In the regression analysis, dactylitis ($p = 0.042$) and high serum CRP levels ($p = 0.004$) predicted glucocorticoid use (Table 2).

Taking into account factors associated with the dose and duration of glucocorticoids, it has been observed that patients with dactylitis and high levels of CRP, DAS-38, and DAPSA were using higher doses of glucocorticoids ($p = 0.034$, $p = 0.003$, $p = 0.031$, and $p = 0.021$). High TJS ($p = 0.000$), SJS ($p = 0.027$), high serum CRP levels (0.006), and high DAS-28 ($p = 0.000$) and DAPSA ($p = 0.000$) levels were associated with glucocorticoid use longer than 3 months. The use of high-dose glucocorticoids correlated with long-term treatment with glucocorticoids ($p = 0.000$) (Table 3).

Treatment outcomes

Fifty-three (37.5%) patients (36% of female patients and 42% of male patients) had sustained remission for 52 weeks on cDMARD monotherapy (Fig. 1). It was observed that remission-LDA continued for at least 24 weeks after treatment was discontinued in 16 of 55 patients who used glucocorticoids. There was no difference between the sexes who are in remission on DMARD monotherapy ($p = 0.300$) or glucocorticoids ($p = 0.087$).

During this 2-year follow-up, 33 patients were started on TNF inhibitors. In 2 patients who experienced exacerbation after TNF inhibitor, disease activity was controlled with short-term (< 3 months) use of glucocorticoids.

No psoriasis flare-up was observed in any patient after cessation of glucocorticoid treatment.

Discussion

This study showed that one-third of psoriatic arthritis patients used glucocorticoids, and one-third of them had sustained remission-low disease activity (LDA) after cessation of glucocorticoids. In the vast majority of patients, it was sufficient to use glucocorticoids at low doses and

Table 1 Clinical differences between genders

Variable	Female ($n = 96$)	Male ($n = 45$)	*P* value
Age (mean, SD)	50.44 ± 13.76	46.87 ± 12.76	0.144
Symptom duration (mean, SD)	2.96 ± 6.05	3.77 ± 6.51	0.474
DIP involvement (*n*,%)	14 (14%)	3 (6%)	0.142
Large joint involvement (*n*,%)	24 (25%)	11 (24%)	0.560
TJS (mean, SD)	4.76 ± 2.67	3.98 ± 3.11	0.127
SJS (mean, SD)	3.74 ± 1.99	3.02 ± 2.2	0.056
VAS (mean, SD)	5.94 ± 1.13	5.69 ± 1.04	0.214
DAS 28 (mean, SD)	3.56 ± 0.62	3.36 ± 0.75	0.088
CRP (mg/dL) (mean, SD)	13.7 ± 13.5	13.7 ± 12.2	0.996
DAPSA (mean, SD)	21.80 ± 6.79	19.97 ± 8.12	0.164
Uric acid (mg/dL) (mean, SD)	4.67 ± 1.33	6.53 ± 1.38	0.000*
Enthesitis (*n*, %)	11 (11%)	6 (13%)	0.473
Dactylitis (*n*, %)	9 (9%)	3 (6%)	0.429
Axial involvement (*n*, %)	19 (19%)	11 (24%)	0.337
Cervical vertebrae involvement (*n*, %)	10	3	0.354
Sacroiliitis (uni-bilateral) (*n*, %)	11 (11%)	12 (26%)	0.023*
Nail psoriasis (*n*, %)	8 (8%)	0 (0%)	0.042
Pustular psoriasis (*n*, %)	3 (3%)	2 (4%)	0.513
Non-psoriasis (*n*, %)	8 (8%)	2 (4%)	0.325
TNF inhibitor (*n*, %)	16 (16%)	17 (37%)	0.006*
GC use (*n*, %)	42 (43%)	13 (28%)	0.66
GC dose < 7.5 mg (*n*)	38	9	0.054
7.5–30 mg (*n*)	4	4	
> 30 mg (*n*)	0	0	
GC duration			0.159
< 3 months (*n*)	37	10	
> 3 months (*n*)	5	3	

DIP distal interphalangeal joint, *TJS* tender joint count, *SJS* swollen joint count, *VAS* visual analogue scale, *CRP* C reactive protein, *DAS-28* disease activity score-28, *DAPSA* Disease Activity Index for Psoriatic Arthritis, *TNF* tumor necrosis factor, *GC* glucocorticoid

*Significance ($P \leq 0.05$ is statistically significant)

Table 2 Multiple regression analysis for glucocorticoid use

Variable	*p*	OR/β coefficient	95.0% confidence ınterval	
			Lower bound	Upper bound
Gender	0.06	0.63	0.367	1.1
DIP involvement	0.161	1.75	0.72	4.28
Enthesitis	0.522	1.09	0.44	2.70
Dactylitis	0.042	3.12	0.98	9.89
Axial involvement	0.365	1.19	0.63	2.26
Sacroiliitis (uni-bilateral)	0.248	0.68	0.301	1.55
Nail psoriasis	0.33	0.521	0.109	2.49
Pustular psoriasis	0.351	0.39	0.04	3.407
CRP	0.004	0.299	0.004	0.019
DAS-28	0.366	0.227	− 0.195	0.526
DAPSA	0.331	− 0.231	− 0.047	0.016
Uric acid (mg/dL)	0.134	0.124	− 0.012	0.087

Analysis adjusted for age and symptom duration. *DIP* distal interphalangeal joint, *CRP* C reactive protein, *DAS-28* disease activity score-28, *DAPSA* Disease Activity Index for Psoriatic Arthritis, *OR* odds ratio

*Significance ($P \leq 0.05$ is statistically significant)

Table 3 Correlation analysis with glucocorticoid dose and duration

Variable	Dose	Duration
Age	0.057	0.197
Gender	0.054	0.159
Duration	0.292	0.298
DIP involvement	0.139	0.327
Large joint involvement	0.962	0.962
Enthesitis	0.065	0.480
Dactylitis	0.034*	0.630
Axial involvement	0.503	0.609
Nail psoriasis	0.628	0.628
Pustular psoriasis	0.645	0.645
TJS	0.264	0.000*
SJS	0.300	0.027*
CRP	0.003*	0.006*
DAS 28	0.031*	0.000*
DAPSA	0.021*	0.000*
GC dose	NA	0.000*
GC duration	0.000*	NA

DIP distal interphalangeal joint, *TJS* tender joint count, *SJS* swollen joint count, *CRP* C reactive protein, *DAS-28* disease activity score-28, *DAPSA* Disease Activity Index for Psoriatic Arthritis, *GC* glucocorticoid

*Significance ($P \leq 0.05$ is statistically significant)

for less than 3 months. The frequency of use of glucocorticoids, the dose, and the duration were similar in men and women. Dactylitis and high serum CRP levels were predictive factors for the administration of glucocorticoids. While rates of cDMARDs response and glucocorticoid use were similar between genders, the use of TNF inhibitors was higher in male patients. No patient developed erythroderma or severe pustular psoriasis during follow-up or after discontinuation of glucocorticoid therapy.

The efficacy and retention rates of methotrexate in RA and PsA patients appear to be similar, and it is the first-line treatment option for both conditions [16]. In addition to methotrexate, glucocorticoids are also frequently used in the therapy of RA, both as a bridging therapy and on a long-term basis. On the other hand, the data on the use of glucocorticoids in psoriatic arthritis is not as extensive and clear as in rheumatoid arthritis. Aimo et al investigated the frequency of glucocorticoid use by Latin-American rheumatologists in psoriatic arthritis and the indications for the use of the drug [17]. Ninety-four percent of doctors stated that they prescribe glucocorticoids in PsA patients. In the majority of patients, glucocorticoids were administered at doses below 10 mg and for short periods of time. Clinical indications for glucocorticoid therapy were; peripheral arthritis (79%), dactylitis (23%), enthesitis (20%), cutaneous involvement (11%), and axial involvement (8%). In another study, glucocorticoids have been shown to be effective in axial involvement in psoriatic arthritis, axial inflammation in patients with PsA responds better to corticosteroids (triamcinolone acetonide 80 mg) than in patients with AS [18]. Glucocorticoids are recommended conditionally only in peripheral arthritis in the EULAR-GRAPPA guidelines [7, 8]. In light of these recommendations, our study only included patients taking glucocorticoids to control peripheral arthritis, other indications were excluded from the study.

Despite all the available data, physicians often hesitate to use glucocorticoids in PsA patients because of the risk

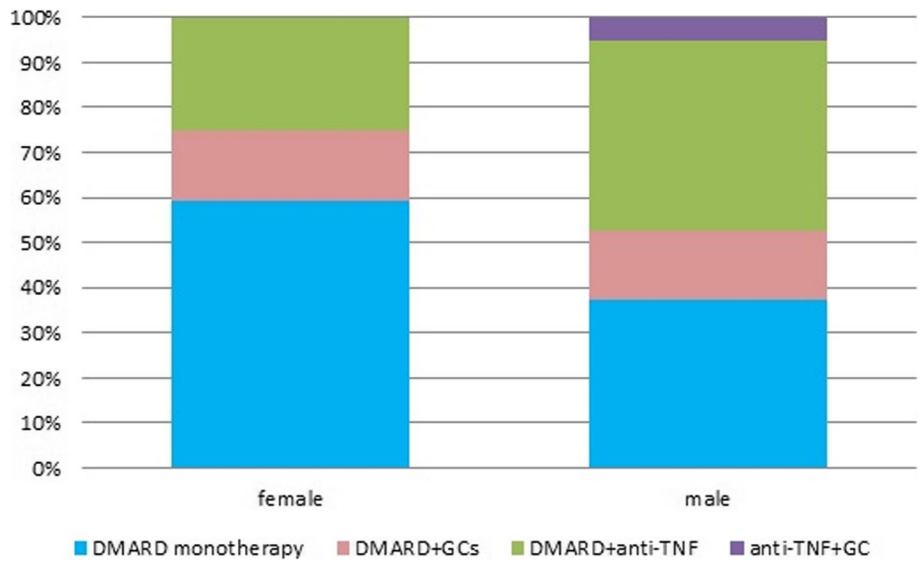

Fig. 1 Treatment and gender distribution of patients who were in remission-low disease activity in 2 years follow-up

of psoriasis flares upon discontinuation. A cohort study of 1970 patients, following the administration of systemic corticosteroids only 1.42% of patients had psoriasis flares [19]. A systemic review also showed that observational or interventional studies did not report an increased risk or occurrence of psoriatic flares related to systemic glucocorticoid use [20]. In our study, no flare in psoriasis (including pustular, erythrodermic, and worsening plaque psoriasis) was observed in any patient after glucocorticoid cessation.

PsA is currently recognized as a disease that affects both sexes equally [21]. Few studies have examined the role of gender in PsA, and results vary. Gender differences in PsA include more frequent axial involvement in males [22] and predominant peripheral arthritis with higher disability scores in females [23]. Female patients with PsA are less likely to develop radiographic damage in axial and peripheral joints than male patients [24]. There are also various studies reporting that there are differences between genders in treatment responses. Passia et al showed that after 3 months cDMARD therapy, 77% of the women retained their methotrexate as the dominant drug, while it was 88% in men [25]. According to data from Danish Health Care Registers, male patients respond better to TNF inhibitor treatments [11]. The study also showed that male patients had longer TNF inhibitor persistence than females (3.8 years versus 1.4 years). In our study, we observed that sacroiliac joint involvement was more common in males and serum uric acid levels were higher. However, we did not observe any gender differences in cDMARD responses and glucorticoid intake.

The main limitation of the study is that it is an observational study. However, since treatment guidelines do not routinely recommend the use of glucocorticoids and there is no clear indication of when to start them or for what dose and duration they can be used, it is worth evaluating real-world data. We also did not assess psoriatic skin lesions, but patients with predominant psoriatic skin involvement were excluded at baseline. Treatment was carried out only for psoriatic arthritis.

Conclusion

About one-third of PsA patients used glucocorticoid therapy in 2-year follow-ups and one-third of them had long-term remission-low disease activity (LDA) even after cessation of glucocorticoids. There were no differences in cDMARD response and the frequency of glucocorticoid use between genders. Low-dose short-term prednisolone seems to be a reasonable choice for the control of peripheral arthritis in PsA patients. In our opinion, the addition of glucocorticoids to cDMARDs as a bridging therapy in PsA patients should be evaluated in randomized controlled trials.

Abbreviations

ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
BUN	Blood urea nitrogen
CASPAR	ClASsification criteria for Psoriatic ARthritis
CBC	Complete blood count
CI	Confidence interval
CRP	C-reactive protein
cDMARD	Conventional Disease-Modifying Anti-rheumatic Drugs
DAPSA	Disease Activity Index for Psoriatic Arthritis
DAS28-CRP	Disease activity was measured using the Disease Activity Scale 28
DIP	Distal interphalangeal
DMARD	Disease-modifying anti-rheumatic drugs
EULAR	European Alliance of Associations for Rheumatology
GC	Glucocorticoid
GRAPPA	Group for Research and Assessment of Psoriasis and Psoriatic Arthritis
LDA	Low disease activity
NSAID	Non-steroidal anti-inflammatory drug
OR	Odds ratio
PsA	Psoriatic arthritis
SJC	Swollen joint count
TJC	Tender joint count
TNF	Tumor necrosis factor
VAS	Visual Analogue Scale

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Not applicable.

Code availability

Not applicable.

Authors' contributions

study conception and design: E.D.B, E.A., I.A.; data collection: E.D.B, E.A.; analysis and interpretation of results: E.D.B., I.A.; draft manuscript preparation: E.D.B, E.A. All authors reviewed the results and approved the final version of the manuscript.

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Availability of data and materials

The data that support the findings of this study are available from the corresponding author, [E.D.BAYRAK], upon reasonable request.

Declarations

Ethics approval and consent to participate

The protocol was approved by the institutional ethics review board of Acıbdem University (protocol number:2023-06/204).

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no conflict of interest.

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