Association of Glucocorticoid Use with Patient-Reported Outcomes among Persons with Systemic Lupus Erythematosus (SLE)

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BACKGROUND

- Glucocorticoids (GCs) have long been a mainstay of treatment for SLE.
- Despite providing benefits, GCs have potential side effects that increase with dose and duration[1] that have the potential to affect quality of life negatively.
- We examined the association of GC use and patient-reported outcomes (PROs).

METHODS

- Data source: Data were provided by adults with SLE in FORWARD with physician-diagnosed SLE from July 2015 – July 2020. FORWARD is a longitudinal registry of individuals with rheumatic diseases. Questionnaires are completed at 6-month intervals.
- Variables: Respondents provided comprehensive health information including GC use and dosage and completed the following PROs:
  - PROMIS Physical Function, Fatigue, Pain Interference, Sleep Disturbance, and Satisfaction with Social Roles; Systemic Lupus Activity Questionnaire (SLAQ); PHQ-8 (depressive symptoms); pain rating (numeric rating, 0 [no pain] – 10 [severe pain]).
  - Worsening in PROs was defined as negative changes from prior to current observation ≥0.5 SD.
  - Changes in GC dose and addition of other medications were assessed from one observation to next. Multiple changes could occur for an individual.
- Observation period:
  - GC users: data were from the questionnaire in which GCs were first reported during observation period. Participants were required to be on GCs for at least one observation period.
  - Non-users: Data drawn from the first questionnaire completed during the observation period.
  - Analyses of worsening required at least two observation periods within a one-year period.
- Analysis: Longitudinal logistic regression analyses used generalized estimating equation (GEE) models to estimate the likelihood of worsening based on increases in GC dose, addition of other medications, or both during the same period. Models controlled for age, sex, race, BMI, comorbidities, education, smoking, SLE duration, self-reported SLE disease activity, and self-reported SLE organ damage (Brief Index of Lupus Damage, BILD).

RESULTS

- Of 424 participants eligible for analysis with ≥2 consecutive observations, 49.3% reported GC use in at least one 6-month period.
- GC users were less likely to be male or white, had more comorbidities, had longer SLE duration, and reported more active SLE and greater disease damage (BILD) (**Table 1**).
- GC users (compared to non-users) had worse scores on all PROs at baseline (**Table 1**).
- Medication changes were rare in the no GC use group (no changes in 97% of observations; **Table 2**).
- The majority of GC users also had no medication changes (83% of observations). Increases in GC dose were noted in 11.3% of observations, other medications added in 4.5% and both GC increases and medication additions in 1.5% (**Table 2**).
- Increases in GC dose, addition of other medications, or the combination were not associated with PRO worsening (**Table 3**). The exception was for PHQ, for which there was a significant likelihood of higher scores in the group with increase in GC plus addition of another medication.

Glucocorticoid use in SLE was associated with worse PROs initially, but not with further worsening over time

Table 1. Characteristics of FORWARD participants by GC use/non-use

Variable	No GC use (n=215)	GC use (n=209)	p-value
Dose of GC 0 - <5 mg/day 5 - <10 mg/day ≥ 10 mg/day		10.1 (43) 25.5 (108) 13.7 (58)	
Male sex	7.9 (17)	3.4 (7)	0.03
White, non-Hispanic	87.4 (188)	76.6 (160)	0.003
Age, years	58.4 ± 13.0	60.1 ± 12.8	0.15
Education, years	14.4 ± 2.6	14.7 ± 2.0	0.19
College graduate	47.9 (103)	49.8 (104)	0.70
General health characteristics			
Rheumatic Disease Comorbidity Index (0 – 9)	2.4 ± 1.9	2.8 ± 1.9	0.03
BMI, kg/m^2	28.6 ± 7.5	29.4 ± 8.7	0.35
Ever smoked	35.8 (77)	30.6 (64)	0.26
SLE characteristics			
SLE duration, years	23.7 ± 12.5	26.4 ± 13.3	0.03
How active is your lupus today (0 – 10 rating)	2.3 ± 2.4	3.4 ± 2.8	0.000
BILD (Brief Index of Lupus Damage) score	2.9 ± 1.9	3.9 ± 2.3	0.000
Medications			
Hydroxychloroquine	61.4 (132)	59.3 (124)	0.66
Immunosuppressives*	17.7 (38)	41.6 (87)	0.000
Patient-Reported Outcomes (PROs)			
PROMIS Physical Function	45.9 ± 9.4	40.4 ± 9.3	0.000
PROMIS Fatigue †	52.5 ± 11.4	58.1 ± 10.7	0.000
PROMIS Pain Interference †	54.3 ± 9.9	58.4 ± 9.4	0.000
PROMIS Sleep Disturbance †	52.0± 9.0	55.7 ± 9.4	0.000
PROMIS Satisfaction with Social Roles †	50.9 ± 10.1	46.2 ± 9.5	0.000
SLAQ † (Systemic Lupus Activity Questionnaire) †	3.8 ± 3.8	5.6 ± 4.4	0.000
PHQ(Patient Health Questionnaire)-8 (depressive symptoms) †	4.8 ± 4.5	6.9 ± 5.5	0.000
Pain rating, 0 (no pain) – 10 (severe pain) †	3.4 ± 3.0	4.5 ± 2.8	0.000

Tabled values are % (n) or mean ± SD. P-values from t-tests or chi-square analyses.
PROMIS scores reported as T-scores (population mean ± SD, 50 ± 10).
* Immunosuppressive medications included azathioprine, mycophenolate, methotrexate, cyclosporine, leflunomide, cyclophosphamide, rituximab, belimumab, or other biologics.
† Higher scores are worse.

Table 2. Observation time and frequency of medication changes

	Observation time (years)		Medication changes, % (n)			
			Increase GC	No change	Add other medications	Both
No GC use	3.0 ± 2.3	N observations	---	97.1 (1743)	2.8 (51)	---
GC use	3.4 ± 2.2	N observations	11.3 (120)	83.0 (1314)	4.5 (71)	1.5 (23)

Table 3. Likelihood of worsening in PROs by medication changes

Patient-reported outcomes	N observations	N people	Medication changes		
			Increase GC	Add other medications	Both
PROMIS Physical Function	1984	355	0.8 (0.4, 1.6)	0.9 (0.4, 1.6)	2.3 (0.6, 7.9)
PROMIS Fatigue †	1988	355	0.9 (0.5, 1.5)	1.3 (0.8, 2.2)	1.6 (0.5, 5.8)
PROMIS Pain Interference †	1758	358	1.2 (0.7, 2.1)	0.9 (0.4, 1.8)	1.0 (0.2, 4.3)
PROMIS Sleep Disturbance †	1963	354	0.8 (0.4, 1.3)	1.3 (0.8, 2.1)	1.2 (0.3, 4.5)
PROMIS Satisfaction with Social Roles †	1973	357	1.3 (0.9, 2.1)	1.4 (0.7, 2.6)	2.0 (0.6, 7.0)
SLAQ † (Systemic Lupus Activity Questionnaire) †	2321	359	0.9 (0.6, 1.3)	1.0 (0.6, 1.7)	2.1 (0.6, 6.7)
PHQ-8 (depressive symptoms) †	2576	400	1.4 (0.9, 2.1)	1.1 (0.6, 1.9)	**2.6 (1.2, 5.7)**
Pain rating (0 – 10) †	2958	424	1.0 (0.6, 1.4)	1.0 (0.6, 1.7)	1.3 (0.4, 3.9)

Tabled values are odds ratios (95% confidence intervals) from multiple regression analyses controlling for age, sex, BMI, education, smoking, SLE duration, and self-reported SLE organ damage (measured by BILD, Brief Index of Lupus Damage)
† Higher scores are worse.

CONCLUSION

- GC use was associated with worse PROs at the baseline for these analyses.
- Results suggest that patients tend to remain on relatively stable GC doses over time despite potential side effects. Patients may be willing to risk negative side effects of GC to avoid further worsening of symptoms such as pain or fatigue.
- In this non-inception cohort with relatively long disease duration, PROs generally did not worsen over time with changes in GC dosage or other medications; i.e., the differences between GC users and non-users appeared to be static over time.

[1] Katz P, et al. Association of glucocorticoid use with healthcare utilization among persons with SLE. Arthritis Rheum 2022; 74 (suppl 9), abstract 0995.

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The National Databank for Rheumatic Diseases