The Journal of Rheumatology 2020;47:xxxx
doi:10.3899/jrheum.201137
First Release October 15 2020

The Journal of Rheumatology

Letter

Long-term Glucocorticoid Use in Rheumatoid Arthritis

To the Editor:

We read with interest the article by Hanly and Lethbridge concerning long-term patterns of glucocorticoid (GC) use in older patients with rheumatoid arthritis (RA)[1]. Their report indicates that GC use has remained relatively stable over time, in contrast to greater use of disease-modifying antirheumatic drugs and biologic agents in the treat-to-target directive. They also report that rheumatologists prescribe lower doses than other physicians, and that the mean dose for rheumatologists has decreased over time.

The discussion decries continued use of GC, stating that in view of "the risks associated with chronic corticosteroid use, especially in older adults, renewed efforts are required to minimize their use in the long-term pharmacological management of RA."[1] Of course, we fully agree that chronic dosing of prednisone (in North America, or prednisolone in Europe) in doses above 5 mg/d is generally undesirable. However, we find the blanket recommendation to discontinue GC entirely in RA unfortunate, in view of compelling evidence that doses of 5 mg/d prednisone or less provide effective and safe therapy, and has been of benefit to many patients with RA.

A recent placebo-controlled trial indicated that even patients in minimal disease activity or remission while taking tocilizumab on 5 mg/d prednisone suffered more flares when their prednisone was slowly tapered over a period of 16 weeks, and fully discontinued for only 8 weeks[2]. This phenomenon is consistent with older data that documented the efficacy of 3 mg/day prednisone in a withdrawal clinical trial[3], and similar effectiveness in most patients of an initial and ongoing dose of 3 mg prednisone to doses ≥ 5 mg/day[4]. Further, in 75 patients with RA treated with prednisone in doses < 5 mg for 4 to 8 years and in 73 patients for more than 8 years, the only clinically important adverse events were bruising and thinning of the skin, with no greater prevalence of hypertension, cataracts, or diabetes than expected[4]. Flares were rarely seen, possibly due to continuous control of inflammation by not discontinuing GC at all. Finally, 4 reports published before 1990 indicated that adrenal corticoid suppression was rare in patients taking 5 mg/d prednisolone and not seen in lower doses in those taking less than 5 mg/d[5,6,7,8].

A large placebo-controlled trial on 2 years of 5 mg/d prednisolone in seniors (65+ yrs) with RA will present results next year that can hopefully provide further support for continued small doses over long periods, if not indefinitely[9]. The diathesis leading to RA does not disappear, just as in diabetes and hypertension, and that is why therapy must be continued indefinitely in almost all patients.

In 2002, an editorial concerning a clinical trial documenting efficacy of 10 mg/day prednisolone versus placebo asked, "Are long-term very low doses of prednisone for patients with RA as helpful as high doses are harmful?"[10] It was suggested that "a little corticosteroid, like a glass of wine may benefit many people, whereas a high dose...like a bottle of wine is harmful to all"; and also that "additional disease-modifying antirheumatic drugs [to prednisolone] appeared to be required."[10] Experience over 18 subsequent years has reinforced these concepts. Very low-dose GC has an excellent benefit-to-harm ratio and frequently provides optimal control for patients with RA.

Maarten Boers[1], MSc, MD, PhD
Theodore Pincus[2], MD
[1]Epidemiology & Data Science, and Amsterdam Rheumatology and Immunology Center, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam, the Netherlands;
[2]Rush University, Chicago, Illinois, USA.

Dr. Pincus is president of Medical History Services LLC, and holds a copyright and trademark on the Multidimensional Health Assessment Questionnaire (MDHAQ) and the Routine Assessment of Patient Index Data (RAPID3), for which he receives royalties and license fees, all of which are used to support further development of quantitative questionnaire measurement for patients and doctors in clinical rheumatology care.

Address correspondence to Dr. T. Pincus, Rush University, 1611 West Harrison Street, Suite 510, Chicago, IL 60612, USA.
Email: tedpincus@gmail.com.

REFERENCES

1. Hanly JG, Lethbridge L. Disease modifying antirheumatic drugs, biologics and corticosteroid use in older patients with rheumatoid arthritis over 20 years. J Rheumatol 2020 Aug 1 (in press).
2. Burmester GR, Buttgereit F, Bernasconi C, Alvaro-Gracia JM, Castro N, Dougados M, et al. Continuing versus tapering glucocorticoids after achievement of low disease activity or remission in rheumatoid arthritis (SEMIRA): a double-blind, multicentre, randomised controlled trial. Lancet 2020;396:267-76.
3. Pincus T, Swearingen CJ, Luta G, Sokka T. Efficacy of prednisone 1-4 mg/day in patients with rheumatoid arthritis: a randomised, double-blind, placebo controlled withdrawal clinical trial. Ann Rheum Dis 2009;68:1715-20.
4. Pincus T, Sokka T, Castrejon I, Cutolo M. Decline of mean initial prednisone dosage from 10.3 to 3.6 mg/day to treat rheumatoid arthritis between 1980 and 2004 in one clinical setting, with long-term effectiveness of dosages less than 5 mg/day. Arthritis Care Res 2013;65:729-36.
5. Danowski TS, Bonessi JV, Sabeh G, Sutton RD, Webster MW Jr, Sarver ME. Probabilities of Pituitary-Adrenal Responsiveness after Steroid Therapy. Ann Intern Med 1964;61:11-26.
6. Daly JR, Myles AB, Bacon PA, Beardwell CG, Savage O. Pituitary adrenal function during corticosteroid withdrawal in rheumatoid arthritis. Ann Rheum Dis 1967;26:18-25.
7. Wood JB, Frankland AW, James VH, Landon J. A rapid test of adrenocortical function. Lancet 1965;1:243-5.
8. LaRochelle GE Jr, LaRochelle AG, Ratner RE, Borenstein DG. Recovery of the hypothalamic-pituitary-adrenal (HPA) axis in patients with rheumatic diseases receiving low-dose prednisone. Am J Med 1993;95:258-64.
9. Hartman L, Rasch LA, Klausch T, Bijlsma HW, Christensen R, Smulders YM, et al. Harm, benefit and costs associated with low-dose glucocorticoids added to the treatment strategies for rheumatoid arthritis in elderly patients (GLORIA trial): study protocol for a randomised controlled trial. Trials 2018;19:67.
10. Pincus T, Sokka T, Stein CM. Are long-term very low doses of prednisone for patients with rheumatoid arthritis as helpful as high doses are harmful? Ann Intern Med 2002;136:76-8.