RHEUMATOID ARTHRITIS

The entangled effects of RA and glucocorticoids on glucose metabolism

An investigation of the effects of glucocorticoid therapy for rheumatoid arthritis (RA) on glucose metabolism has found that metabolic parameters are comparable between users and non-users of these drugs. Large daily or cumulative doses were, nevertheless, associated with type 2 diabetes mellitus (T2DM); however, it is unclear whether the drugs caused T2DM or were associated with it as a consequence of being prescribed more frequently in active RA (itself associated with insulin resistance). Overall, “the findings confirm the mild toxicity profile that we believe low-dose glucocorticoids have in RA,” declares Jos Hoes, an author of the paper published in *Annals of the Rheumatic Diseases*.

Glucocorticoids—named for effects on glucose metabolism, including stimulation of gluconeogenesis—are a mainstay of DMARD combination therapy for chronic RA, and are implicated in the associated increase in cardiovascular disease risk. Nevertheless, “the role of glucocorticoids in this process is ambiguous,” explains Hoes, “since on the one hand they could increase these negative cardiovascular effects of the disease through their negative effects on carbohydrate metabolism, but on the other hand they could decrease them through their anti-inflammatory action.”

Hoes and colleagues enrolled 82 glucocorticoid-naïve and 58 current glucocorticoid users from among patients

Glucocorticoids suppress RA-associated inflammation—which can cause insulin resistance—but alter glucose metabolism. Whether high-dose glucocorticoids cause T2DM or are associated with it because they are prescribed in active RA is unclear.

with RA of ≥ 2 years with no known T2DM, as well as 50 controls with normal glucose metabolism. Insulin sensitivity and secretion in the fasted state were calculated using validated indices, and dynamic tests (frequently-sampled oral glucose tolerance tests) were used to probe postload insulin sensitivity and β -cell function. Statistical analysis revealed associations of these metabolic parameters with drug dose and disease characteristics.

Insulin sensitivity and β -cell function were similar between patients with RA who had or had not received glucocorticoids, and were impaired in patients in comparison with controls. Levels of previously undiagnosed T2DM or impaired glucose metabolism suggested that these problems are currently underestimated in RA. Incident T2DM

was associated with prednisolone dose (OR cumulative dose 1.04, $P=0.002$; daily dose 1.13, $P=0.13$), but less so after adjustment for disease activity.

The results are good news for users of low-dose glucocorticoids, but the complex relationship between chronic, high-dose glucocorticoid therapy, RA and T2DM remains to be unravelled.

Emma Leah

Original article Hoes, J. N. et al. Glucose tolerance, insulin sensitivity and β -cell function in patients with rheumatoid arthritis treated with or without low-to-medium dose glucocorticoids. *Ann. Rheum. Dis.* doi:10.1136/ard.2011.151464

Further reading Hoes, J. N. et al. Current view of glucocorticoid co-therapy with DMARDs in rheumatoid arthritis. *Nat. Rev. Rheumatol.* 6, 693–702 (2010)