RHEUMATOID ARTHRITIS

Do steroids increase metabolic syndrome risk?

Despite the widespread availability of glucocorticoids for the treatment of rheumatoid arthritis (RA), their long-term cardiovascular safety has been questioned. Driven by evidence indicating an increased prevalence of cardiovascular disease risk factors in RA, investigators from the UK have now explored a potential link between long-term glucocorticoid use and the metabolic syndrome. Although definitive diagnostic criteria have not been developed, the metabolic syndrome is generally characterized as a collection of classic cardiovascular risk factors.

“...the beneficial effects produced by glucocorticoids ... may outweigh the harmful effects”

In their well-characterized cross-sectional cohort of 398 patients with RA, Tracey Toms *et al.* identified 117 patients taking either low-dose (<7.5 mg per day) or medium-dose (≥7.5 mg per day) glucocorticoids for more than 6 months. In these patients, the metabolic syndrome was characterized according to the US National Cholesterol Education Program III, the most up-to-date and widely used criteria for the diagnosis of metabolic syndrome. The investigators

identified significant associations between long-term glucocorticoid therapy and just two of the individual components of the metabolic syndrome, namely hypertension and triglyceride levels. When all the individual components were combined, no associations were found between long-term glucocorticoid use and the metabolic syndrome, even after adjusting for potential confounders, such as age, disease duration and disease activity index. However, “This was a cross-sectional study, so any inferences of causality or directionality of the associations found should be seen with caution”, explains Toms, who is based at the Dudley Group of Hospitals NHS Trust, Dudley, UK.

Toms’ team suggests that this lack of an observed relationship between glucocorticoid exposure and the metabolic syndrome could be related to the effects of systemic inflammation resulting from RA itself. Any further contributions to increased cardiovascular risk from glucocorticoids, such as increased HDL cholesterol levels or alterations in body fat/muscle distribution, might, therefore, be redundant. Conversely, explains Toms, “it is possible that the beneficial effects produced by glucocorticoids [in] suppressing the impact of inflammation on the metabolic syndrome may outweigh the harmful effects”.

US National Cholesterol Education Program III criteria for the metabolic syndrome

The presence of **at least three** of the following features:

- Fasting plasma glucose ≥6.1 mmol/l, or on drug treatment for elevated blood glucose
- Systolic blood pressure ≥130/85 mmHg
- Triglyceride level ≥1.7 mmol/l or drug treatment for elevated triglyceride level
- HDL cholesterol level: males <1.0 mmol/l; females <1.3 mmol/l
- Waist circumference: males >102 cm; females >88 cm

More studies are needed to “tease out [the] further complexities of cardiovascular disease in RA,” says Toms. “This work has acted as a springboard, prompting interest into the effects of other drugs both on the metabolic syndrome and cardiovascular risk factors as a whole.”

Negin Nassabeh

Original article Toms, T. E. *et al.* Lack of association between glucocorticoid use and presence of the metabolic syndrome in patients with rheumatoid arthritis: a cross sectional study. *Arthritis Res. Ther.* **10**, R145 (2008).