The influence of HDL-cholesterol and CRP on increased insulin resistance and impaired beta-cell function in patients with rheumatoid arthritis

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Background: Increased CRP in RA patients is associated with lower levels of HDL cholesterol. HDL cholesterol may enhance insulin secretion and stimulate glucose uptake into skeletal muscle, adipose tissue, and liver. Objectives: To investigate whether lower HDL, alone or in combination with CRP, could explain increased insulin resistance (IR) and impaired beta-cell function in RA patients compared to healthy controls.

Methods: The study population included 127 non-diabetic subjects (90 RA patients and 37 matched controls). We determined body mass index, waist circumference (WC), and presence of metabolic syndrome (MetS). All patients were on disease modifying antirheumatic drugs, 65.6% on steroids (none on steroids >10 mg/day), and 27.8% on biological therapy. Laboratory analyses included hsCRP, glucose, insulin, and C-peptide (as a marker of insulin secretion). Insulin resistance (IR) was calculated using the updated Homeostasis Model Assessment (HOMA2-IR), based on fasting plasma glucose and specific insulin concentrations. The output of the HOMA2 model was calibrated to give IR of 1 as normal. HOMA2-B indicates the potential of beta-cells to compensate increased IR. Lack of compensatory rise of HOMA2-B implied impaired beta-cell function.

Results: IR was detected in 74.4% of RA patients and in 54.2% controls, p=0.025. RA patients had significantly higher concentration of specific insulin, C peptide, and HOMA2-IR than controls, while HOMA2-B was not statistically different. Both groups were comparable regarding all other factors known to affect glucose metabolism (age, WC, presence of MetS). We found significant differences in inflammation markers between RA patients and controls: ESR 29.5 (14-44) vs. 16.0 (10.0-20.0); hsCRP 5.5 (2.8-15) vs. 3.0 (1.8-3.9); p<0.000 for both, as well as in lipids, especially HDL concentration 1.5±0.4 vs 1.60±0.3, p=0.027 and a number of differences for HOMA2-IR and insulin became less important but still persisted (Table), while significance for C peptide became more prominent. When we added the influence of inflammation, this favourable effect of HDL-cholesterol on C-peptide disappeared.

Conclusions: RA patients had higher IR and impaired beta-cell function in comparison to healthy controls. The augmentation of statistical significance for C peptide, as a marker of insulin secretion, after adjustment for low HDL-cholesterol and significant effect of HDL on logHOMA2-B implicate its important role in disturbances of glucose metabolism in RA.

Disclosure of Interest: None declared