High Inflammation May Condition the Antiatherogenic Function of Small, Dense HDL in Patients with Active Rheumatoid Arthritis.

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Background/Purpose: Rheumatoid arthritis (RA) is associated with increased mortality, mainly due to cardiovascular disease. High grade inflammation might drive to premature atherosclerosis. High-density lipoprotein (HDL) possesses multiple biological activities, including antioxidative actions. Small, dense HDL3c particles exert potent antiatherogenic activities, which can be compromised under conditions of chronic inflammation. It remains indeterminate as to whether the level of such functional HDL deficiency is related to the degree of inflammation. Our objective was to evaluate HDL antioxidative function in normolipidemic RA active patients and controls.

Methods: serum from normolipidemic female patients with active RA (DAS28 _3.2; n_12) and normolipidemic age-matched female controls (n_10) was analized. Plasma levels of total cholesterol (TC), triglycerides (TG), HDL, LDL, apo-A, apo-B, plasma C-reactive protein (PCR), and serum amyloid A (SAA), subfractions of LDL and HDL were obtained. Small, dense HDL3b and 3c particles were isolated by density gradient ultracentrifugation. The capacity to protect LDL from oxidative stress induced by free radicals was assessed in small, dense HDL3b and HDL3c subpopulations, and in total HDL.

Results: sera from 12 active female RA patients and 10 age-matched female controls were analized. No significant differences were observed in plasma levels of TC, TG, LDL, HDL, apo-A and apo-B. Active RA patients exhibited a wide range of plasma C-reactive protein (CRP) levels, which were elevated relative to controls (8.4 mg/l, CI 3.5–11.4 vs. 0.47 mg/l, CI 0.30–0.89, p_0.001). Antioxidative activity and total chemical composition of small, dense HDL did not differ between RA patients and controls (p_0.05). Nonetheless, subgroup analyses revealed that RA patients featuring high levels of inflammation (CRP_10mg/l) possessed small, dense HDL with reduced antioxidative activities (up to _23%, p_0.01). Furthermore, antioxidative activity of HDL was inversely correlated with plasma CRP and SAA levels. HDL3b and 3c were depleted of free cholesterol (FC) in high-inflammated RA patients. This FC depleted HDL particles were less efficient in preventing LDL oxidation.

Conclusion: only RA patients who displayed high circulating levels of inflammatory biomarkers (CRP and SAA) possessed small, dense HDL3 particles with reduced antioxidative activity. This reduction in antioxidative action of HDL3 particles, along with reduced capacity of HDL to promote cholesterol efflux, and depletion of free cholesterol in HDL, may enhance development of atherosclerosis in active RA patients. These pathophysiological features are intimately linked to the inflammatory state, supporting that uncontrolled chronic inflammation leads to increased cardiovascular risk.