Improvement of cell cholesterol trafficking-related lipoprotein function in rheumatoid arthritis patients treated with tocilizumab

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Background/Objectives: Rheumatoid Arthritis (RA) is associated with accelerated atherosclerosis, partly attributed to disturbances in serum lipoprotein functions. Tocilizumab treatment, targeting IL-6, is increasingly being used in RA but its effects on circulating lipoproteins, including a decrease in totalhigh density lipoproteins (HDL), are generating some concerns about its possible pro-atherogenic effect. We studied serum HDL capacity to promote cell cholesterol efflux (CEC) in RA patients before and after tocilizumab treatment.

Design/Method:serum was drawn from 8 patients with RAbefore (t0) and after 4(t1) and 12(t2) weeks of intravenoustreatment (8 mg/Kg/4 weeks).CEC was measured with radioisotopic technique and standardized cell models distinguishing between cholesterol effluxmediated by the membrane transporters Scavenger receptor Class B type I (SR-BI) andATP binding cassette A1 and G1 (ABCA1 and ABCG1), each of which interacts preferentially with specific HDL subfractions.

Results:SR-BI-mediated CEC increased significantly after treatment (mean ± SEM 2.43 ± 0.33, 2.88 ± 0.30, 3.41 ± 0.35 at t0, t1 and t3 respectively; $p=0.025$ t0 vs t1, $p=0.008$ t0 vs t3) while total HDL serum levels were unmodified, so that the ratio SR-BI-mediated CEC/HDL levels increased significantly ($p<0.05$ t0 vs t3). The same trend, very close to statistical significance (3.97 ± 0.33, 4.44 ± 0.57, 4.97 ± 0.26 at t0, t1 and t3 respectively; $p=0.064$ t0 vs t3) was observed for ABCG1-mediated CEC, while no modification was detected in ABCA1-mediated CEC. Only after treatment an inverse relationship between SR-BI-mediated CEC and ESR appeared, despite the small number of patients.

Conclusions:the results of this pilot study indicate that tocilizumab treatment may improve anti-atherogenic HDL function, known to be impaired in RA.If confirmed in larger studies, thiseffectcould blunt the concern about a negative effect of tocilizumab on cardiovascular risk and, on the contrary, may prove particularly relevant in RA patients with aggressive disease needing anti-IL-6 treatment prone to accelerated atherosclerosis.