Lipids

Circulating levels of proprotein convertase subtilisin/kexin type 9 (PCSK9) are associated with monocyte subsets in patients with stable coronary artery disease

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Background and aims

Proprotein convertase subtilisin/kexin type-9 (PCSK9) is an enzyme promoting the degradation of low-density lipoprotein receptors (LDL-R) in hepatocytes. Inhibition of PCSK9 has emerged as a novel target for lipid-lowering therapy. Monocytes are crucially involved in the pathogenesis of atherosclerosis and can be divided into three subsets. The aim of this study was to examine whether circulating levels of PCSK9 are associated with monocyte subsets.

Methods: We included 69 patients with stable coronary artery disease. PCSK9 levels were measured and monocyte subsets were assessed by flow cytometry and divided into classical monocytes (CD14++CD16-; CM), intermediate monocytes (CD14++CD16+; IM) and non-classical monocytes (CD14 + CD16++; NCM).

Results: Mean age was 64 years and 80% of patients were male. Patients on statin treatment (n = 55) showed higher PCSK9-levels (245.4 (206.0-305.5) ng/mL) as opposed to those without statin treatment (186.1 (162.3-275.4) ng/mL; p = 0.05). In patients on statin treatment, CM correlated with circulating PCSK9 levels (R = 0.29; p = 0.04), while NCM showed an inverse correlation with PCSK9 levels (R=-0.33; p = 0.02). Patients with PCSK9 levels above the median showed a significantly higher proportion of CM as compared to patients with PCSK-9 below the median (83.5 IQR 79.2-86.7 vs. 80.4, IQR 76.5-85.2%; p = 0.05). Conversely, PCSK9 levels >median were associated with a significantly lower proportion of NCM as compared to those with PCSK9 <median (10.2, IQR 7.3-14.6 vs. 14.3, IQR 10.9-18.7%; p = 0.02). In contrast, IM showed no association with PCSK-9 levels.

Conclusions: We hereby provide a novel link between PCSK9 regulation, innate immunity and atherosclerotic disease in statin-treated patients.