Evaluation of endothelial progenitor cells as cardiovascular prognostic biomarkers in hemodialysis patients

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Background Endothelial cells arise from endothelial progenitor cells (EPCs), which reside in bone marrow vascular niches, and are classified according to specific functional differences. Oxidative stress and inflammation lead to endothelial dysfunction that is a critical event in the initiation and progression of atherosclerotic plaques. Patients with chronic renal failure frequently show endothelial dysfunction and are at a greatly increased risk of developing atherosclerosis. Owing to their ability to partially restore vascular damage, both the number and functional changes in EPCs may be considered as useful prognostic biomarkers of cardiovascular events in hemodialysis (HD) patients.

Purpose This study investigated EPC features and several biomarkers of systemic vascular inflammation and carotid atherogenesis in hemodialysis (HD) patients.

Methods We studied 104 HD patients (males=55 and females 49, mean age: 51 ± 12 years) and 40 healthy controls (males=20/females=20; mean age: 52 ± 11 years). Isolated EPCs were cultured in the fibronectin-covered culture dishes and counted. EPC markers were studied by flow cytometry (FACS) by using anti-CD34, anti-CD133 and anti-vascular endothelial growth factor receptor 2 (VEGFR-2) antibodies. Serum levels of intercellular cell adhesion molecule (ICAM), vascular cell adhesion molecule (VCAM), IL-6, TNF-a, and asymmetric dimethyl-arginine (ADMA) were measured by ELISA method. Carotid intima-media thickness (CIMT) and ratio (CIMR) were also evaluated.

Results In our experimental conditions, EPC number was decreased in HD patients when compared to controls (p < 0.01). Expression of CD34 was significantly lower in the HD group (p < 0.01). Interestingly, EPCs were significantly inversely correlated with serum TNF-a levels in HD patients (r= -0.388, p < 0.01) but not in the control group (r = -0.133, p = NS). Furthermore, there was an inverse association between VEGFR-2 positive cells and serum TNF a levels (r= -0.401, p = 0.002) in HD patients. In HD patients, there was a positive correlation between ICAM levels with CIMT (r = 0.405, p = 0.03) and CIMR was positively correlated with VCAM levels (r = 0.377, p = 0.01) and ADMA (r= 0.233, p<0.05).

Conclusions Our study shows that EPC number was decreased in HD patients and it was associated with systemic inflammation. TNF-a could activate inhibitory actions on EPC in HD patients. A significant relationship was present between ICAM/VCAM and carotid atherosclerosis, while this was not evident with EPC number. These pathogenic mechanisms can contribute to the high incidence of cardiovascular diseases in HD patients. However, further larger studies should investigate this working hypothesis.