GENDER DIFFERENCES IN PPAR-GAMMA EXPRESSION IN MONOCYTE/ MACROPHAGES FROM CORONARY ARTERY DISEASE (CAD) PATIENTS

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Peroxisome proliferator-activated receptor-gamma (PPAR-gamma) is expressed in a wide variety of cells, including human monocytes, macrophages and foam cells, which are deeply involved in atherosclerosis. PPAR-gamma is activated by naturally occurring ligands, including 15-deoxy-delta_12,14_prostaglandin J_2 (15-deoxi-PGJ_2) and ox-LDL, as well as by synthetic agents, such as the thiazolidinedione antidiabetic drugs. This study was aimed to evaluate PPAR-gamma expression in monocytes (M) and monocyte-derived macrophages (MDM) from CAD patients, smokers and non-smokers, and to look for a possible gender difference.

M were collected from heparinised venous blood from 20 males and 20 females with CAD by standard techniques and purified by adhesion; MDM were prepared from M cultured for 8-10 days in RPMI 1640 medium enriched with 20% FCS. PPAR-gamma constitutive expression was evaluated by immunoblotting and expressed as PPAR-gamma/beta-actin ratio.

Our results indicate that the basal expression of PPAR-gamma increased during differentiation from M to MDM and was significantly higher in CAD non-smoker patients as compared to CAD smoker patients (p<0.05). Since women have a lower prevalence and incidence of cardiovascular events compared with men and the mechanisms responsible for this gender-specific difference are unclear, we evaluated PPAR-gamma expression in CAD men and women, smokers and non-smokers. In non-smoker patients, PPAR-gamma expression was significantly higher (p<0.005) in female M and MDM (n=15) as compared to male cells (n=15). Smoker women (n = 5) presented a constitutive reduced PPAR-gamma expression as compared to non-smoker women. Interestingly, PPAR-gamma expression during differentiation was lower in smoker women as compared to smoker men (n=5) and reached statistical significance in MDM (p<0.05). A significant inverse correlation (p<0.05) between LDL levels and PPAR-gamma expression was observed in male M, but only a marginal correlation in female M. Total cholesterolemia, HDL and triglyceridemia seemed to be correlated with PPAR-gamma expression in male M and MDM, even if they did not reach statistical significance. In addition, a more intriguing situation was documented in female M and MDM.

This study indicates the existence of a gender difference in PPAR-gamma expression and suggests PPAR-gamma as a possible biomarker for CAD.