

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

AMORUSO ANGELA¹, BARDELLI CLAUDIO¹, RIBICHINI FLAVIO², FERRERO VALERIA², VASSANELLI CORRADO², BRUNELLESCHI SANDRA¹

¹Dept. Med. Sciences, University A. Avogadro, Novara, Italy;

² Division Cardiology, University of Verona, Italy

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 J₂ (15-deoxi-PGJ₂) 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.