THE EFFECT OF OXIDATIVE STRESS ON THE EXPRESSION OF PAI-1, t-PA, u-PA AND u-PAR IN VASCULAR ENDOTHELIAL CELLS

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Plasminogen activator inhibitor type-1 (PAI-1) is the primary inhibitor of tissue-type and urokinase-type plasminogen activators and play integral role in the control of the fibrinolytic system. High plasma PAI-1 level is a risk factor for thrombotic diseases such as myocardial infraction, stroke, and venous thromboembolism. PAI-1 is an early response gene known to be activated by hormones, cytokines, lipoprotein, angiotensin II, phorbol ester, and reactive oxygen species (ROS). The purpose of the present study was to establish whether or not an enhanced oxidative stress involving endothelial injury, activation of coagulation, and inflammatory reaction would induce an expression of PAI-1, t-PA, u-PA or u-PAR.

Human endothelial cells were treated with hydrogen peroxide (100, 200 μM), sodium nitroprusside (1 mM) and oxidative stress were determined by lucigenin chemiluminescence and 2',7'-dichlorofluorescein (DCF) fluorescence, respectively. PAI-1, t-PA, u-PA and u-PAR transcription were determined by transfection of PAI-1, t-PA, u-PA and u-PAR promoter linked to a luciferase reporter. Ap1, HIF-1 and NFκB activity was determined by an electrophoresis mobility shift assay. Expression of PAI-1, t-PA, u-PA and u-PAR in vascular endothelial cells studied using microarray assay and confirmed by real time PCR.

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