The Role of NO in the Progression and Regression of Atherosclerosis via Endothelial Senescence

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Nitric oxide(NO) bioavailability is limited in senescence. We studied it in human umbilical venous endothelial cells (HUVECs). NO donor and transfection with endothelial NO synthase(eNOS) into HUVECs each decreased SA-b-gal positive cells and increased telomerase activity. 17 β -estradiol decreased SA-b-gal-positive cells and caused cell proliferation. L-arginine(L-Arg) or L-citrulline(L-Cit) partially inhibited, and combination of L-arg and L-cit(LALC) strongly prevented, high glucose-induced senescence. Following 3-day stimulation of HUVECs under high-glucose with L-Arg or L-Cit or LALC, endothelial senescence and function were evaluated. These amino acids were also administered to dyslipidemic type 2 diabetic(ZDFM) rats fed a high-cholesterol diet for 4 weeks. L-Cit and LALC retarded HG-induced endothelial senescence, and restored telomerase activity. p22-phox was not altered, but L-Cit decreased ROS. Under HG, L-Cit and LALC increased NO. and eNOS and phosphorylated eNOS were decreased. In ZDFM rats, SA-b-gal on the aortic surface was reduced by L-Cit and LALC. LALC for 4 weeks increased plasma NO. Thus, L-Cit and LCLA inhibited HG-induced endothelial senescence and NO-cGMP pathway. The delay in endothelial senescence through NO and eNOS may have clinical utility in the treatment of atherosclerosis in elderly.