Carvedilol Inhibits Tumor Necrosis Factor- -induced Endothelial Transcription Factor Activation, Adhesion Molecule Expression, and Adhesiveness to Human Mononuclear Cells.

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摘要

Abstract

Objective— We tested the hypothesis that carvedilol, a ß-adrenoceptor and -adrenoceptor antagonist with potent antioxidant property, could inhibit tumor necrosis factor- (TNF-)–induced endothelial adhesiveness to human mononuclear cells (MNCs), an early sign of atherogenesis.

Methods and Results— Circulating MNCs were isolated from the peripheral blood of healthy subjects. Compared with control condition, pretreatment of carvedilol (10 µmol/L for 18 hours) or probucol (5 µmol/L for 18 hours), but not propanolol, prazosin, or both propanolol and prazosin significantly decreased TNF-–stimulated adhesiveness of cultured human aortic endothelial cells (HAECs) to MNCs. Carvedilol inhibited TNF-–stimulated endothelial vascular cell adhesion molecule-1 (VCAM-1) and E-selectin (66.0±2.0% and 55.60±1.0% of control, P<0.05, respectively) expression, whereas probucol inhibited only VCAM-1 expression (79.0±5.0% of control, P<0.05). Propanolol, prazosin, or both did not alter the expression of adhesion molecules. Further, pretreatment with carvedilol significantly inhibited TNF-–stimulated intracellular reactive oxygen species (ROS) production and the activation of redox sensitive nuclear factor kappa B and activator protein-1 transcription pathways.

Conclusions— Carvedilol reduced TNF-–stimulated endothelial adhesiveness to human MNCs by inhibiting intracellular ROS production, transcription factor activation, and VCAM-1 as well as E-selectin expression, suggesting its potential role in clinical atherosclerosis disease.

Carvedilol, a ß- and -adrenoceptor antagonist, could prevent endothelial adhesiveness to human mononuclear cells by inhibiting intracellular reactive oxygen species production, redox-sensitive transcription pathways, and vascular cell adhesion molecule-1 and E-selectin expression in TNF-–stimulated human aortic endothelial cells, suggesting its potential role in clinical atherosclerosis disease.

Key Words: antioxidant • atherosclerosis • carvedilol • cell adhesion molecules • endothelium