IJAE
Vol. 123, n. 1 (Supplement): 67, 2018
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

Endothelial progenitor cells senescence is accelerate by ROS Urea-induced

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Cardiovascular disease is one of the leading contributors to morbidity and mortality in chronic renal failure (CRF) patients. Endothelial injury caused by various cardiovascular risk factors is a responsable for atherosclerosis [1]. In uremic patients, evidence of endothelial dysfunction has been identified at early stages of the disease [2]. Endothelial progenitor cells (EPCs) play a key role in the maintenance of vascular integrity by promoting endothelial repair mechanisms and new endothelial growth. Uremia and compromised renal function are associated with a greater reduction in EPC availability and function [3]. Here we investigate the hypothesis that increased concentrations of urea associated with CRF increase ROS production directly in EPCs, causing abnormalities associated with coronary artery disease risk. Human EPCs were isolated from peripheral blood mononuclear cells of healthy donors and cultured in the presence or absence of 20 mmol/L urea. Urea, at concentrations seen in CRF, induces reactive oxygen species production in endothelial progenitor cells through the activation of mitochondrial and cytosolic mechanisms. Urea-induced ROS production impairs EC-CFU morphology and number, reduced the uptake and binding of Dil-Ac-LDL and lectin-1, and the ability to differentiate into CD31- and vascular endothelial growth factor receptor 2 positive cells. Moreover, urea-induced ROS generation accelerated the onset of EPC senescence, leading to a senescence-associated secretory phenotype (SASP). Normalization of mitochondrial ROS production prevented each of these effects of urea. These data suggest that urea itself causes both reduced EPC number and increased EPC dysfunction, thereby contributing to the pathogenesis of cardiovascular disease in CRF patients.

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Key words

Urea, EPC, ROS.