

HIGH GLUCOSE INDUCED HUMAN PERITONEAL MESOTHELIAL CELL APOPTOSIS AND MITOCHONDRIAL DYSFUNCTION

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Continuous ambulatory peritoneal dialysis is convenient as one of the renal replacement therapy for end-stage-renal-disease patients. The bio-incompatible peritoneal dialysis solutions are bearing characteristics of high glucose, hyperosmolality, and low pH value, may lead to the development of peritoneal fibrosis. The glucose of currently used peritoneal dialysis solutions is 1.5% (84mM), 2.5% (138mM), and 4.25% (236mM), respectively. Long-term exposure of human peritoneal mesothelial cells (HPMCs) to high glucose condition will result in changes of peritoneal structure and physiological function, and causing the HPMCs to fall off gradually and cell death. To study damage to the HPMCs of CAPD patients, we examined whether glucose overload accelerates mitochondrial damage and HPM cell apoptosis in vitro. A dose-dependently increase in cell apoptosis in were demonstrated in high glucose exposed HPMC. The dissipation of mitochondrial membrane potential were found in high glucose exposed HPMC. In addition, the enhanced reactive oxygen species (ROS), lipid peroxides (as thiobarbitic acid-reacted malondialdehyde), and 8-hydroxy-deoxyguanosine(8-OH-dG) were identified in HPMC cultured in high glucose. Concurrently, confocal microscopy revealed the localization of lipoperoxide and 8-OH-dG to mitochondria. Transmission electron microscopy showed swelling of mitochondria and cell vacuolization in high glucose treated HPMCs. Obviously, an increase of PARP cleavage, caspase-9 and caspase-3 activation, and collagen production were detected in high glucose exposed HPMC. The n-acetylcysteine treatments significantly attenuated high glucose-induced cell apoptosis. These data suggest that high-glucose may cause oxidative damages, mitochondrial damages, and activate apoptosis signal transduction pathways leading to cell casualties.

Key word:

high glucose, human peritoneal mesothelial cells