題名:N-Acetylcysteine-Mediated Antioxidation Prevents Hyperglycemia-Induced Apoptosis and Collagen Synthesis in Rat Mesangial Cells.

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摘要:BACKGROUND/AIMS: High-glucose (HG)-induced mesangial apoptosis and fibrogenesis possibly involves reactive oxygen species (ROS) formation and activated mitochondrial stress. We investigated the therapeutic effect of the antioxidant N-acetylcysteine (NAC) on cellular apoptosis and matrix accumulation in HG-treated rat mesangial cells (RMCs). METHODS: RMCs were cultured in media containing 5 (control) or 35 mM (HG) glucose. Cellular apoptosis was assayed by TdT-mediated dUTP nick-end labeling staining. Collagen and transforming growth factor-1 gene expression were measured by reverse transcriptase-polymerase chain reaction or Northern blotting. Mitochondrial capacity and intracellular ROS generation was assayed by fluorescence microscopy and flow cytometry, respectively. Cellular ATP production and malondialdehyde (MDA) formation were determined by a luciferin-luciferase reaction and high-performance liquid chromatography, respectively. Cytochrome c release, caspase activation and poly(ADP)ribose polymerase cleavage were assayed by Western blotting. RESULTS: HG-treated RMCs displayed enhanced cellular apoptosis (65%) and collagen gene expression (1.8-fold increase); these reactions could be significantly suppressed by 1 mM NAC ($p < 0.05$). Intracellular ROS generation, production of ATP and MDA, and caspase-3, -8 and -9 activities were significantly increased in HG-treated RMCs, and were effectively attenuated by addition of NAC. CONCLUSION: It is concluded that NAC prevents HG-induced mesangial apoptosis and fibrogenesis

pathways by the reduction of oxidative stress.