S-C12

Nicotine Induces Apoptosis in Human Proximal Tubular Cells

Joon Seok Choi[1], Soo Yeon Joo[2], Hoon In Choi[2], Chang Seong Kim[1]
Eun Hui Bae[1], Seong Kwon Ma[1], Jong Un Lee[2], Soo Wan Kim[1]

Department of Internal Medicine[1] Chonnam National University Medical School
Department of Physiology[2] Chonnam National University Medical School

Background: Cigarette smoking is considered as independent risk factor for progression of chronic kidney disease and nicotine is the major compound of cigarette. The present study was aimed to investigate the effect of nicotine on renal tubular epithelial cell apoptosis in vitro and explore the potential mechanisms involved.
Methods: Human proximal tubular epithelial (HK-2) cells were treated with 200 μM of nicotine. Cell viability was examined using MTT assay. The DCF-DA staining was used to measure intracellular levels of reactive oxygen species (ROS). The protein expression of extracellular signal-regulated kinase (ERK), P38 and c-Jun N-terminal kinase (JNK), NF-κB, Bax and Bcl-2 was determined by semiquantitative immunoblotting.
Results: Nicotine treatment resulted in dose-dependent decreases of cell viability and increases of ROS. Nicotine increased the expression of p-ERK, p-JNK and p-P38. Nicotine induced expression of p-ERK and p-JNK in HK-2 cells, which was attenuated by pretreatement of N-acetyl-cysteine. The expression of NF-κB started to increase 1 hour after nicotine exposure. Increased nuclear NF-κB activation was counteracted by inhibitors of ERK (PD98059) or JNK (SP6 00125), but not affected by p38 MAPK inhibitor (SB203580). Nicotine decreased the expression of Bcl-2, while increased that of Bax, which was attenuated by the treatment of NF-κB inhibitor (Bay 11-7082) or N-acetyl-L-cysteine (NAC). Flow cytometry analysis revealed nicotine-induced apoptosis.
Conclusion: These results suggest that nicotine induce apoptosis by increased ROS generation through activation of NF-κB and mitogen-activated protein kinase signaling pathways in HK-2 cells.

Key Words: Nicotine, Apoptosis, Reactive oxygen species