KSN 2017 Abstract

KSN-17-O012 [FMC 연구비]

Puromycin aminonucleoside induces podocyte apoptosis by endoplasmic reticulum stress

*Tae-sun HA, Seo-yoon MIN

Pediatrics, College of Medicine Chungbuk National University, Korea,South

Objectives : Puromycin aminonucleoside (PAN) is known to be a podocytotoxin, therefore, PAN-induced nephrosis is a widely studied animal model of human idiopathic nephrotic syndrome. Endoplasmic reticulum (ER) stress is the common findings under various pathogenic microenvironments, contributing to the progression of various podocyte diseases. Abnormal protein accumulation associated with ER stress in the ER of podocytes produces structural and functional damage in the cells, which in turn leads to podocyte apoptosis and severe proteinuria. In the present study, we investigated the effect of PAN on ER stress and apoptosis in in vitro podocytes.

Methods : We cultured rat and mouse podocytes and treated with various concentrations of PAN and evaluated ER stress markers by western blotting and apoptosis by FACS and TUNEL assays.

Results : PAN treatment increased ER stress markers, such as, ATF6 and caspase-12 at 12 and 24 hrs, in a dose-dependent manner, which were improved by chemical chaperones, such as, sodium 4-phenylbutyric acid (PBA) and TUDCA. PAN also induced podocyte apoptosis significantly in concentration- and time-dependent manners in FACS and TUNEL assays, which were improved by Nox4 siRNA, ATF6 siRNA, and chemical chaperones. LY294002, a PI3-kinase inhibitor, exaggerated ER stress and apoptosis significantly. Therefore, PAN induced ER stress, thereafter, increased oxidative stress, subsequently induced podocyte apoptosis by the inhibition of PI3-kinase signaling.

Conclusions : Our studies suggest that PAN could induce podocyte ER stress of mainly ATF6 and caspase-12 pathways, which would contribute to the development of podocyte apoptosis by oxidative stress and inhibiting PI3-kinase survival signaling.

Keywords : Puromycin aminonucleoside; Endoplasmic reticulum stress; Nephrotic syndrome; Proteinuria; Oxidative stress; Podocyte; apoptosis