S-C10

HK-2 세포에서 4-Hydroxy-2-hexenal에 의한 염증과 섬유화 및 Paricalcitol의 효과

전남대학교 의과대학 내과[1], 전남대학교 의과대학 생리학과[2]

김창성[1], 주수연[2], 김혜진[2], 서미나[1], 류지나[1], 최준석[1], 배은희[1], 마성권[1], 이종은[2], 김수완[1]

Paricalcitol Attenuates 4-Hydroxy-2-hexenal-induced Inflammation and Fibrosis in Human Renal Proximal Tubular Epithelial Cells

Chang Seong Kim[1], Soo Yeon Joo[2], Hyejin Kim[2], Mi Na Seo[1], Ji Na Ryu[1]
Joon Seok Choi[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: 4-hydroxy-2-hexenal (HHE), which is the aldehyde product of lipid peroxidation, might be responsible for the pathogenesis of renal mitochondrial dysfunction and apoptosis. Recently, paricalcitol (19-nor-1, 25-dihydroxyvitamin D2) is renoprotective in various experimental nephropathy models through its anti-inflammatory and anti-fibrotic actions. We investigated the effects of paricalcitol on inflammation and fibrosis after HHE-induced renal tubular epithelial cell injury.

Methods: HK-2 cells were cultured with 10 μM of HHE in the absence or presence of paricalcitol. To investigate the underlying molecular mechanisms of HHE-induced tubule cell inflammation, we examined the nuclear factor-κB, mitogen-activated protein kinase (MAPK), and the inflammatory protein iNOS and COX-2 in human proximal tubular epithelial (HK-2) cells. Also, we evaluated the Wnt/β-catenin signaling, TGF-β1/Smad signaling, fibrotic protein CTGF and fibronectin to investigate the fibrosis and its signaling mechanism. The protein expression was determined by semiquantitative immunoblotting.

Results: In HHE-treated HK-2 cells, paricalcitol attenuated the increases of the expression of phospho-p38 MAPK, phospho-extracellular signal-regulated kinase (p-ERK) and phospho-c-Jun N-terminal kinase (p-JNK), and also prevented the activation of nuclear factor-κB. The HHE-induced increased the expression of iNOS and COX-2, as well as CTGF and fibronectin, were attenuated by paricalcitol treatment. The HHE treatment resulted in a time-dependent increase of the expression of β-catenin, whereas paricalticol reduced its expression in HHE-treated HK-2 cells. In addition, HHE increased the expression of the TGF-β1 and Smad-4 which were attenuated by the treatment of paricalcitol.

Conclusions: Paricalcitol appears to attenuate HHE-induced renal tubular cell injury by suppression of inflammation and fibrosis through inhibition of the nuclear factor-κB, MAPK and Wnt/ β-catenin signaling pathways.

Key Words: 4-hydroxy-2-hexanal, 섬유화, HK-2세포
4-hydroxy-2-hexanal, Fibrosis, HK-2 cells, Inflammation, MAPK