F-C16

Indoxyl sulfate가 혈관 내피세포 기능부전에 미치는 영향

김정혜 · 신경숙 · 유민아 · 류정화 · 류동열 · 강덕희

이화여자대학교 의과대학 신장내과

Indoxyl Sulfate (IS) : Is it a New Player of Endothelial Dysfunction in Patients with Chronic Renal Failure (CRF)?

Kim Jung Hye, Shin Kung Sook, Yu Mina, Ryu Jung Hwa, Ryu Dong Ryeol, Kang Duk Hee

Ewha Womans University College of Medicine Nephrology

Introduction : The major cause of mortality in patients with CRF patient is cardiovascular disease, however the pathophysiologic mechanism of the development and aggravation of cardiovascular disease is not completely understood. Endothelial dysfunction (ED) is the earliest phenomenon of atherosclerotic vascular disease which is the consequence of decreased NO bioavailability, oxidative stress and endothelial cell senescence. IS is one of the uremic toxin that accelerates the progression of renal disease, however there have been limited studies about the effect of IS on other organ including cardiovascular system. To explore the effect of IS on endothelial dysfunction with its mechanism, we performed *An in vitro* study to investigate the effect of IS on endothelial cell proliferation, apoptosis, NO release, ROS generation and cell senescence.

Methods : IS (25 & micro; g/mL, 125 & micro; g/mL)-induced changes in endothelial cell proliferation was assessed by MTS assay and cell counting in primarily isolated human umbilical venous endothelial cells (HUVEC). HUVEC apoptosis was evaluated by Annexin V staining and FACscan analysis. NO release was measured by ELISA with analysis of phosphorylation of endothelial nitric oxide synthase (eNOS). Intracellular ROS generation in HUVECs was measured by DCF-DA staining and FACscan analysis. Endogenous eNOS inhibitor, asymmetric dimethylarginine (ADMA) production was measured by high-performance liquid chromatography (HPLC). For detection of cell senescence, cells were fixed and stained for senescence-associated β-galactosidase (SA β-gal) activity.

Results : IS inhibited serum-induced endothelial cell proliferation at 24 and 48 hours of incubation. IS increased HUVEC apoptosis at 24 hours. IS decreased NO release (17% vs. control) associated with a decreased eNOS phosphorylation (41% vs. control) and an increased ADMA production. ROS generation was also significantly increased in HUVEC treated with IS at 30 minutes (200% vs. control). IS increased SA β-gal activity at 48hours.

Conclusion : Our study suggests an increased level of IS in CRF patients may play an important role in endothelial dysfunction via decreasing NO bioavailability, generation of oxidative stress and inducing endothelial cell apoptosis and senescence. Further studies to examine the effect of lowering IS on markers or mediators of endothelial dysfunction will be necessary.