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글루코사민이 저산소증에 노출된 신장 근위세뇨관세포의 소포체 스트레스와 SGLT 기능 약화에 미치는 영향

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Glucosamine Attenuates ER Stress and Dysfunction of SGLT During Hypoxia Via Akt and GSK-3beta in Renal Proximal Tubule Cells

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There is growing body of data demonstrating that the increase of protein O-linked N-acetylglucosamine (O-GlcNAc) has been shown to increase cytoprotection following oxidative stress. Therefore, the goal of this study was to determine whether glucosamine (GlcN) could ameliorate endoplasmic reticulum (ER) stress-induced dysfunction of Na+/glucose cotransporter (SGLT) in renal proximal tubule cells (PTCs) under hypoxia. Hypoxia-induced reactive oxygen species (ROS) stimulated ER stress ascertaining with the expressions of glucose-regulated protein 78 (GRP78) and C/EBP-homologous protein (CHOP) and phosphorylation of eukaryotic initiation factor 2 alpha (eIF2a) in a time dependent manner. Hypoxia decreased the levels of protein O-GlcNAc, expressions of O-GlcNAc transferase (OGT) and SGLTs, and [14C]-a-methyl-D-glucopyranoside (a-MG) uptake. In order to mitigate the decreases of protein O-GlcNAc and OGT expression under hypoxia, we treated GlcN which significantly restored protein O-GlcNAc level and OGT expression. Moreover, GlcN and PUGNAc (an inhibitor of O-GlcNAcase) inhibited hypoxia-induced ER stress protein expressions and ameliorated dysfunction of SGLTs and a-MG uptake. In experiment to elucidate how GlcN attenuated ER stress, GlcN increased phosphorylation of Akt to inactivate glycogen synthase kinase 3 beta (GSK3b) by phosphorylation at Ser9. Furthermore, when PTCs were treated with Akt inhibitor, GlcN could not reverse hypoxia-induced ER stress response and decreases of SGLT expression and a-MG uptake. Taken together, these data suggest that GlcN with increased level of protein O-GlcNAc ameliorated hypoxia-induced ER stress to maintain SGLT activity through Akt and GSK-3b in renal PTCs.

Key Words: 저산소증, 글루코사민, 소포체스트레스
Hypoxia, Glucosamin, Endoplasmic Reticulum (ER) Stress