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HK2 세포에서 PGC-1a 과발현에 의한 NF-kB의 활성 조절과 산화스트레스생성의 저해

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Adenovirus Gene Transfer of PGC-1α Decreases ROS Generation in HK2 Cells Via Reducing NF-κB Activation

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Purpose: The Peroxisome Proliferator Activated Receptor (PPAR) gamma Co-activator 1α (PGC-1α) is a transcriptional coactivator identified as a regulator of intracellular reactive oxygen species (ROS) level and mitochondrial biogenesis. Ischemia/reperfusion (I/R) triggers acute kidney injury via aggravating oxidative stress and inflammation. Therefore we postulated PGC-1α may reduce oxidative stress and inflammation in renal tubule cells.

Method: We used an adenovirus vector to transfer PGC-1α. Human proximal tubular epithelial (HK-2) cells were treated with 100 MOI (multiplicity of infection) of adenovirus containing PGC-1α gene (Ad-PGC-1α) or control adenovirus devoid of PGC-1α (Ad-Null) were cultured for 24 hr. The fluorescent probe 2',7'-dichlorofluorescein diacetate was used to measure intracellular levels of reactive oxygen species (ROS). The expression of antioxidant related gene was measured by real time PCR. The protein expression of NF-κB was determined by immunoblotting.

Result: Superoxide dismutae 2 (SOD2) mRNA expression was most significantly increased after PGC-1α overexpression. We also confirmed that mRNA expression of mitochondria transcription factor A (mtTFA) and catalase has been increased after PGC-1α overexpression. Uncoupling protein 2 (UCP2) mRNA expression has been reduced by H_2O_2 treatment, which was counteracted by induction of PGC-1α overexpression. To confirm antioxidant effect of PGC-1α, we measured ROS level. H_2O_2 treatment increased ROS level up to 2 times, while PGC-1α significantly reduced ROS level in HK-2 cells. Oxidative stress also induced NF-κB activation. We confirmed PGC-1α overexpression reduced NF-κB p65 subunit nucleus localization in HK-2 cells.

Conclusion: PGC-1α reduced oxidative stress in HK2 cells via reducing ROS generation and NF-κB activation, suggesting that PGC-1α may have role to prevent acute kidney injury via inhibition of oxidative stress.

Key Words: PGC1-a, 산화스트레스, HK2 세포, NF-kB, PGC-1α, Oxidative stress, ROS, Acute kidney injury