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허혈재관류 신손상 마우스에서 미토콘드리아 표적 물질의 신보호 효과

충남대학교병원[1], 대전성모병원[2]

최대은[1], 정진영[1], 최현수[2], 장윤경[2], 정사라[1], 나기량[1], 이강욱[1]

A Novel Mitochondria-targeted Antioxidant Compound Attenuates Ischemia Reperfusion Renal Injury

Dae Eun Choi[1], Jin Young Jeong[1], Hyun Su Choi[2], Yoon Kyung Chang[2]
Sarah Chung[1], Ki Ryang Na[1], Kang Wook Lee[1]

Chungnam National University Hospital[1]
Daejeon Saint Mary Hospital[2]

Introduction: Recently mitochondrial damage has been known to major role in various renal injury including ischemia reperfusion (IR) renal injury. Mitochondrial injury and reactive oxygen species (ROS) generation play a role in IR renal injury. NecroX-7 is recently developed compounds which are concentrated in mitochondria, reduce mitochondrial reactive oxygen species and improve cell survival. We therefore used NecroX-7, one of these compounds, and assessed its effects on renal damage.

Methods: in vitro, IR was simulated by mineral oil in HK-2 cells. Mitochondrial respiratory complex, membrane potential, and reactive oxygen generation were evaluated in control and IR HK-2 cell with or without NecroX-7. Cell survival also evaluated. In vivo 10 weeks C57BL/6 mice were divided into 4 groups; vehicle (n=5) and NecroX-7 (10 mg/kg intraperitoneal injection) treated sham group (n=5), vehicle n=7)d NecroX-7(n=7) with IR (reperfusion 27 minutes after clamping of both renal artery and vein) renal injury. Kidneys and blood were harvested 24hr after IR injury. We performed real time RT-PCR, western blot and immunohistochemistry for molecular study and H&E stain and PAS stain for histologic examination.

Results: NecroX-7 treatment significantly increase survival of IR HK-2 cell. NecroX-7 treatment increase mitochondrial complex IV and oxygen consumption rate. Also it decrease the 3NT and 8-OH deoxyguanosine generation. in vivo, The levels of BUN and serum creatinine in IR renal injury with NecroX7 treated mice were significantly lower than that of vehicle with IR injured mice ($p < 0.05$). In microscopy, NecroX7 significantly reduced renal tubular epithelial cell necrosis and detachment. NecroX7 significantly reduced 8-OH deoxyguanosine positive and TUNEL positive cells in IR kidney. Also it significantly decreased the level of Bax/Bcl-2 ratio and phosphorylated caspase -3.

Conclusion: In conclusion, NecroX-7 enhance mitochondrial respiratory complex IV and reduce mitochondrial damage and ROS generation. Also it attenuates ischemia reperfusion renal injury.

Key Words: 미토콘드리아, 허혈재관류, 항산화물질
Mitodhondria, Ischemia reperfusion, Antioxidant