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허혈 재관류 신손상 모델에서 에폭사이드 하이드롤라아제의 조절을 통한 치료적 접근

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Pharmacological Modulation of Soluble Epoxide Hydrolase Activity Attenuates Ischemia Reperfusion Injury in Kidney

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Soluble epoxide hydrolase (sEH) in endothelial cells determines the plasma level of epoxyeicosatrienoic acids (EETs) which may control the vascular tone as one of the important vasoactive materials. We hypothesize that the regulation of sE activity may have a therapeutic impact on the extent of the acute kidney injury by the control of EETs level. Ischemia-reperfusion injury (IRI) was induced in C57BL/6 mice by clamping bilateral renal pedicles. sEH activity was controlled by the intraperitoneal administration of 12-(3-adamantan-1-ylureido)-dodecanoic acid (AUDA, 10 mg/kg) or β-cyclodextrin as vehicle. AUDA pre-treatment protected ischemic kidney injury significantly when compared with vehicle treatment (disease control vs. IRI with AUDA: Day 1 Cr 2.93+0.19 mg/dL vs. 2.22+0.31 mg/dL, $p<0.05$; Day 2 Cr 2.65+0.34 mg/dL vs. 1.40+0.51 mg/dL, $p<0.01$). Tubular injury, especially inner medullar area, was significantly attenuated by the administration of AUDA. In biomarker analysis of plasma EpOME and DHOME to investigate the enzyme activity of sEH, the plasma level of EpOME and EpOME/DHOME ratio measured by LC/MS/MS, reflected directly the activity of sEH. In conclusion, the control of sEH activity might be a feasible target for preventing acute kidney injury.

Key Words: 허혈 재관류, 에폭사이드
Ischemia reperfusion, Epoxide