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급성 신장 허혈 관류 모델에서 SIRT1-PGC-1a 신호전달체계를 통한 Resveratrol의 신장보호 효과

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Resveratrol Ameliorates Acute Ischemia/reperfusion Injury in Murine Kidneys by Activating SIRT1-PGC-1α Signaling Pathway

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Background: Ischemia/reperfusion injury (IRI) is a major cause of acute kidney injury (AKI) and an important determinant of long-term kidney dysfunction. Sirtuin1 (SIRT1) is reported to regulate intracellular metabolism and attenuate reactive oxidative species (ROS)-induced apoptosis leading to longevity and acute stress resistance. This study investigated whether activation of SIRT1-PPAR-ɣ coactivator 1α (PGC-1α) signaling by resveratrol (RSV), an activator of SIRT1, would attenuate renal apoptosis and oxidative stress in renal IRI.

Methods: Six to seven-week-old Sprague Dawley (SD) rats were divided into four groups: sham-operated+vehicle (VH), sham-operated+RSV, IRI+VH, and IRI+RSV. Both renal pedicles of SD rats were clamped for 45 min, and sacrificed 48hr after reperfusion. RSV (30 mg/kg) or VH were administered by intraperitoneal injection at 30 min prior to ischemia.

Results: Following the renal IRI, renal function was significantly decreased, which was compatible with histopathologic examination, and it was attenuated by RSV treatment. Serum creatinine at 24hr and 48hr after reperfusion in IRI+VH were 1.87±0.55 and 2.06±1.56, and serum creatinine at 24hr and 48hr after reperfusion in IRI+RSV were 1.19±0.29 and 1.05±1.22 ($p<0.05$). Increased apoptosis measured by cleaved caspase-3 expression after IRI was also significantly decreased with RSV treatment ($p=0.015$). SIRT1 and PGC-1α expression in kidneys was decreased after IRI, and RSV attributed to recover the level of SIRT1 and PGC-1α ($p<0.01$).

Conclusion: The results suggested that RSV protected acute IRI in murine kidney by activation of SIRT1-PGC-1α signaling through modulating renal apoptosis and possibly oxidative stress in the kidney.

Key Words: 급성신부전, 세포자멸사, SIRT1
Scute kidney injury, Apoptosis, SIRT1