KSN 2022
SEOUL, KOREA MAY 26 - 29

Abstract Submission No. : 1180

Effects of poly (ADP-Ribose) polymerase inhibitor treatment on the repair after renal ischemia-reperfusion injury

Junseok Jeon[1], Kyungho Lee[1], Hye Ryoun Jang[1], Jung Eun Lee[1], Ghee Young Kwon[2], Yoon-Goo Kim[1], Dae Joong Kim[1], Wooseong Huh[1]
[1]Department of Internal Medicine-Nephrology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Korea, Republic of
[2]Department of Pathology, Samsung Medical Center, Korea, Republic of

Objectives: Excessive activation of poly (ADP-Ribose) polymerase (PAPR) in the postischemic kidney is one of the crucial pathogenetic mechanisms of ischemic acute kidney injury (AKI). Previous studies reported beneficial effects of PARP inhibition on the early injury phase of renal ischemia-reperfusion injury (IRI), however the role of PARP inhibitions on the repair after renal IRI is yet to be elucidated. The effects of JPI-289, a novel PARP inhibitor, on the healing phase of ischemic AKI were investigated in a murine renal IRI and hypoxic HK-2 cell models.

Methods: IRI surgery was performed on 9-week-old male C57BL/6 mice. Saline (control) or JPI-289 was injected into the peritoneum after IRI. JPI-289 100 mg/kg was administered twice at 24 and 48 hours after unilateral IRI (UIRI), and 50 or 100 mg/kg was administered once at 24 hours after UIRI or bilateral IRI (BIRI). HK-2 cells were treated with the JPI-289 after hypoxic insult.

Results: Renal function was comparable between groups after UIRI, while initially worsened and then recovered in the JPI-289 treated group compared to the control group after BIRI. Renal tubular necrosis and damage, inflammatory cell infiltration, and intrarenal expression of proinflammatory cytokines/chemokines were more prominent in the JPI-289 100 mg/kg twice treated group at 12 weeks after UIRI compared to the control group, although those were comparable between groups at 6 weeks after BIRI or UIRI. The extent of fibrosis was similar between the groups. JPI-289 treatment of 0.5 and 0.75 mg/mL at 3 or 6 hours after hypoxia facilitated the proliferation of hypoxic HK-2 cells, whereas further treatment after 24 hours suppressed proliferation even with lower dosages.

Conclusions: Late treatment of PARP inhibitor after renal IRI did not exert a beneficial effect on the recovery of the ischemic AKI, but may have negative impact on healing.