PARP inhibitor treatment attenuated renal injury in a murine ischemic AKI model

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Objectives: Intrarenal robust inflammatory process following ischemia-reperfusion injury has been reported as the most crucial factor inducing renal injury in ischemic AKI. Although numerous studies investigated various agents of immune modulation as novel treatments for ischemic AKI, few have showed reproducible effects in both animal models and clinical trials. We hypothesized that poly(ADP-Ribose) polymerase (PARP) inhibitor may favorably change post-ischemic intrarenal immunologic micromilieu by decreasing DAMP signal and improve renal outcome in ischemic AKI. The effects of JPI-289 (PARP inhibitor) on early renal injury in a murine ischemic AKI model were investigated.

Methods: Bilateral ischemic-reperfusion injury (BIRI) was induced three groups of 9-week male C57BL/6 mice (control, JPI-289 50mg/kg, and JPI-289 100mg/kg; n=9-10 in each group) by laparotomy approach. Saline or JPI-289 were intraperitoneally injected. Serial changes in renal function were analyzed up to day 3 after BIRI. The effects of JPI-289 on hypoxic HK-2 cells were also investigated.

Results: Renal function deterioration was significantly attenuated in the JPI-289 treatment groups in a dose-dependent fashion. Inflammatory cell infiltration and proinflammatory cytokine expression were also attenuated in the JPI-289 treatment groups. Low dose (0.5 μg/mL) JPI-289 treatment facilitated proliferation of hypoxic HK-2 cells, but very low dose or high dose treatment failed to show favorable effects on hypoxic HK-2 cells.

Conclusions: JPI-289 treatment showed favorable effects by attenuating renal injury in a murine ischemic AKI model and facilitating proliferation of hypoxic HK-2 cells. Further studies are required to elucidate optimal dosage and treatment timing of JPI-289 treatment.