

Abstract Type : Oral

Abstract Submission No. : OR-1225

Role of NLRP3 in rhabdomyolysis-induced acute kidney injury

Yang Gyun Kim¹, Suk-Jong Song¹, Su-Mi Kim¹, Dong-Jin Kim¹, Su-Woong Jung¹, Kyung-Hwan Jeong², Ju-Young Moon¹, Sang-Ho Lee¹

¹Department of Internal Medicine-Nephrology, Kyung Hee University Hospital at Gangdong, Korea, Republic of

²Department of Internal Medicine-Nephrology, Kyung Hee University School of Medicine, Korea, Republic of

Objectives: One study suggested NOD-like receptor, pyrin domain containing-3 (NLRP3) inflammasome contribute renal injury in rhabdomyolysis; however, regarding mechanisms were not clarified. Inflammasome-independent NLRP3 in renal tubular cells might have a vital role in acute kidney injury (AKI). We investigated the role of NLRP3 rhabdomyolysis-induced AKI (RAKI) and evaluated the possibility of NLRP3 as the treatment target of RAKI.

Methods: HK-2 cells and THP-1 cells were treated with ferrous myoglobin to mimic the rhabdomyolysis environment in vitro. A glycerol-injection was executed to the mice to generate RAKI model in NLRP3 knock-out (KO) and wild-type (WT) ones. Selective NLRP3 inhibitor (MCC950) was used as a therapeutic agent.

Results: NLRP3 KO mice showed a marked decrease in serum creatinine, KIM-1, and tubular injury compared with WT mice. NLRP3 deficiency also decreased the magnitude of acute kidney injury. Apoptosis in NLRP3 KO mice was attenuated compared with those of WT mice in case of RAKI. Similarly, inflammatory cytokines, which were increased in WT mice, were mitigated in NLRP3 KO mice. Apoptosis was increased by ferrous myoglobin-induced injury in HK-2 cells. However, it was significantly decreased in siNLRP3-treated HK-2 cells. The NLRP3 inflammasome was activated by ferrous myoglobin in THP-1 cells, and the activity was attenuated by siNLRP3 treatment.

Conclusions: The deficiency of NLRP3 protected kidneys from RAKI by both inflammasome-independent and -dependent ways. The depletion of NLRP3 led to reduce the apoptosis in the renal tubular cell and to mitigate the inflammasome activation in ferrous myoglobin stimulation.