Lowering Serum Uric Acid Attenuated NLRP3 Inflammasome-induced Renal Inflammation in High Fructose Fed OLETF Rat

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Background: The NLRP3 inflammasome is a molecular platform activated upon signs of cellular danger to trigger innate immune defences though the maturation of pro-inflammatory cytokines such as interleukin-1β (IL-1β). Uric acid crystals have recently gained widespread attention due to their role as a natural endogenous adjuvant. Uric acid crystals are internalized and subsequently activate the NLRP3 inflammasome. In this study, we examined the hypothesis that soluble uric acid activates NLRP3 inflammasome-induced renal inflammation in type 2 diabetic rat.

Methods: The LETO and OLETF rats were divided into four groups: (1) LETO group; (2) OLETF group; (3) OLETF+high fructose diet (HFD) group; (4) high fructose fed OLETF with allopurinol treatment (HFD+allopurinol) group. Normal rat kidney proximal tubular epithelial cells (NRK-52E) were also cultured and stimulated with 5 mM uric acid with or without allopurinol.

Results: HFD group showed a higher serum uric acid and urinary albumin creatinine ratio than OLETF group. HFD group showed marked increase of NLRP3 and IL-1β in kidney cortex. Immunohistochemical staining of ED-1 showed significant increase in HFD group compared to OLETF group. Allopurinol attenuated HFD induced hyperuricemia and NLRP3 activation-related renal inflammation. Uric acid also stimulated NLRP3 and IL-1β in NRK-52E cells.

Conclusion: The soluble uric acid could stimulate NLRP3 and IL-1 β in diabetic kidney. It may be related with hyperuricemia induced inflammation and progression of diabetic nephropathy.

Key Words: 요산, 당뇨병성 신증, 염증조절결합체
Uric acid, Diabetic nephropathy, Inflammasome