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Xanthine Oxidase Inhibitor Attenuates TGF-β Expression and Epitherial-mesenchymal Transition in Type 2 Diabetic Nephropathy

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Background : Recently, lowering uric acid (UA) with allopurinol could slow the progression of renal disease in patients with hyperuricemia and chronic kidney disease. In the present study, we hypothesized that the xanthine oxidase inhibitor, allopurinol, attenuate renal injury in type 2 diabetic mice.

Methods : In vivo, KK-Ay/Ta mice were divided into two groups: (1) Control group; (2) Allopurinol group (13 mg/dL in drinking water). In vitro, normal rat kidney tubular epithelial cells (NRK-52E) were stimulated with 1, 5 and 10 mg/dL UA with or without allopurinoll 100 μM.

Results : The allopurinol group showed a lower urinary albumin creatinine ratio than that of the control group. The upregulation of TGF-β and Smad pathway in diabetic kidney was ameliorated by allopurinol treatment. Allopurinol attenuated UA-mediated TGF-β activation in NRK-52E cells. UA-induced mitogen activated protein kinase signaling activation was also attenuated by allopurinol in the NRK-52E cells. The increase of UA-induced a-smooth nuscle actin, vimentin was decreased by allopurinol.

Conclusion : In conclusion, xanthine oxidase inhibitor prevents not only TGF-β and Smad pathway upregulation, but also tubular epitherial-mesenchymal transition. These findings provided a new perspective on the reno-protective effects of the xanthine oxidase inhibitor in diabetic nephropathy.

Key Words : Xanthine oxidase 억제재, 당뇨병성 신증
Xanthine oxidase inhibitor, Diabetic nephropathy, EMT, TGF-β