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Nuclear Factor 2-related Factor 2(Nrf2) Activation Attenuates Renal Fibrosis Induced by Unilateral Ureteral Obstruction in Mice

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Introduction: Renal fibrosis plays an important role in progression of chronic kidney disease. Recent study showed that nuclear factor 2-related factor 2(Nrf2) activation increases glomerular filtration rate in diabetic patients. It is known that oltipraz, Nrf2 activator reduces oxidative stress, inflammation and fibrosis in various animal model includeing liver cirrhosis. We investigated whether oltipraz attenuate renal fibrosis induced by unilateral ureteral obstruction (UUO) in mice.

Methods: Male C57BL/6 mice (8 weeks old, 24-26 g) were divided into 4 groups; sham operated mice, oltipraz-treated sham mice (10 mg/kg, intraperitoneal injection daily), untreated UUO mice, and oltipraz-treated UUO mice. We measured renal expressions of HO-1and Nrf2 1 week after UUO surgery. Light microscopic examination of obstructed kidneys and immunohistochemistry for TGF-β and SMA were performed for the evaluation of renal fibrosis 1 week after UUO.

Results: Renal gene and protein expressions of Nrf2 and HO-1 in oltipraz-treated UUO mice were significantly higher than those of sham operated and UUO mice ($p<0.01$, $p<0.01$). The levels of TGF-β and α-SMA mRNA expression of oltipraz treated UUO mice were significantly lower than those of untreated UUO mice ($p<0.05$). Oltipraz also decreased significantly renal protein expressions of TGF-β and α-SMA in immunohistochemistry compared to untreated UUO mice. Renal F4/80 positive cells in oltipraz treated UUO mice were significantly lower than that of untreated UUO mice ($p<0.05$).

Conclusion: In conclusion, the results of the present study suggest that oltipraz attenuates renal fibrosis induced by unilateral ureteral obstruction in mice.

Key Words: Nrf2, 신섬유화, 요로폐쇄
Nuclear factor 2, Renal fibrosis, Ureteral obstruction