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신절제 쥐 모델에서 Hypoxia-inducible Factor의 단백뇨 감소효과

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HIF Ameliorates Proteinuria in Rat Remnant Kidney Model

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Introduction and Aims : Chronic hypoxia in the kidney has been suggested as a final common pathway to end stage renal disease. Hypoxia- inducible factor (HIF) is a transcription factor regulating cellular hypoxic responses and a promising target for therapeutic potential in the progression of chronic kidney disease. In this study, we investigated the renoprotective mechanism of HIF- 1α in the rat remnant kidney model.

Methods : Sprague- Dawley rats underwent 5/6 nephrectomy or sham operation. Rats were divided into three groups 2 weeks after surgery: 1) sham operated rats with saline infusion (n=5), 2) 5/6 nephrectomized rats with saline infusion (n=7), 3) 5/6 nephrectomized rats with 5 mg/kg/day of prolyl hydroxylase inhibitor dimethyloxalylglycine (DMOG) infusion (n=7). DMOG or saline were continuously administered for 4 weeks using osmotic minipumps. Serum creatinine and proteinuria were measured 6 weeks after surgery. Immunohistochemistry with antibodies against desmin or ED- 1 and semiquantitative immunobloting with antibodies against catalase, caspase, or type IV collagen were performed.

Results : The amount of proteinuria was increased after nephrectomy, but it was significantly reduced by DMOG treatment. GFR was decreased by nephrectomy but was not affected by DMOG treatment. Desmin was prominently immunostained in the nephectomized rats. However, its immunoreactivity was significantly decreased by DMOG treatment. Immunoblotting of catalase and caspase demonstrated that the oxidative stress and apoptosis were ameliorated in DMOG treated group. DMOG treated group had fewer ED- 1- positive cells. Furthermore, the abundance of type IV collagen was markedly reduced by DMOG treatment.

Conclusion : Overexpression of HIF- 1α by DMOG ameliorated the podocyte injury resulting the reduction of proteinuria in rat remnant kidney model. HIF- 1α subsequently attenuated oxidative stress, apoptosis, inflammation and fibrosis in this model.

Key Words : HIF, Proteinuria, 신절제 쥐모델
HIF, Proteinuria, Rat remnant kidney model