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신절제 쥐의 신손상에 대한 Dipeptidyl Peptidase (DPP) IV Inhibitor의 효과

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Dipeptidyl Peptidase (DPP) IV Inhibitor Attenuates Kidney Injury in Rat Remnant Kidney

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Background: DPP IV inhibitors are beneficial for preventing diabetic complications. The aim of this study was to investigate whether DPP IV inhibitor, sitagliptin, could attenuate kidney injury in the rat remnant kidney model.

Methods: After a subtotal nephrectomy, rats were randomly assigned to control or treatment group. Rats in treatement group received food mixed with 200 mg/kg/day of sitagliptin for 8 weeks and then renal injury was evaluated. We measured physiologic data and assessed expression of glucagon-like peptide-1 receptor (GLP-1R), TGF-β, pAKT, AKT and indicators of apoptosis : Bax, cleaved caspase-3, and -9. We performed indirect immunoperoxidase staining with ED-1 to identify macrophages/monocytes and assessed apoptosis by TUNEL assay.

Results: GLP-1R expression was increased in the rat remnant kidneys by sitagliptin treatment (p=0.016). Sitagliptin significantly improved creatinine clearance (CRF vs CRF+sitagliptin : 0.3±0.01 vs 0.4±0.04 ml/min/100 g, p=0.037) and attenuated glomerulosclerosis (score : 3.2±0.6 vs 1.9±0.8, p=0.004) and tubulointerstitial injury (score : 2.7±0.5 vs 1.9±0.6, p=0.019). In addition, sitagliptin markedly reduced the number of apoptotic cells (absolute number: 57.4±12.9 vs 17.6±4.6, p<0.001), and decreased the expression levels of cleaved caspase-3, -9, and Bax in the remnant kidneys (p=0.009, 0.016 and 0.009 respectively).

Conclusion: Our study demonstrated that DPP IV inhibitors improved creatinine clearance and attenuated the degree of histologic injury in the rat remnant kidney model. These renoprotective effects is probably result of decline in apoptosis by activating the GLP-1R.

Key Words: DPP IV 억제제, GLP-1 수용체, 만성 신부전
DPP IV inhibitor, GLP-1 receptor, CKD