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Tacrolimus에 의해 유도된 당뇨 모델에서 Dpp-4억제제의 보호효과

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Dipeptidyl Peptidase-4 Inhibitor Protects Against Tacrolimus-induced Diabetes by Decreasing Oxidative Stress

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Background: Tacrolimus(TAC)-induced diabetes mellitus is one of the important causes of post-transplant diabetes mellitus. This study was performed to evaluate the effect of DPP-4 inhibitor; sitagliptin (STGL) on pancreatic injury caused by TAC.

Method: TAC (1mg/kg/day, SC) with or without STGL (10, 20, 40 mg/kg/day, gavage) were administered to rats for 4 weeks. Body weight and water intake were measured every week. The effect of STGL on TAC-induced pancreatic injury was evaluated by intraperitoneal glucose tolerance test (IPGTT), serum insulin level, and islet size. Area under the curve for glucose (AUCg) was calculated by trapezoidal estimation from the values obtained during the IPGTT, and islet size was measured with insulin-positive area. Oxidative stress was evaluated by measuring serum 8-hydroxy-2'-deoxyguanosine (8-OHdG) level.

Results: After four weeks, co-treatment with STGL was recovered body weight compared with TAC alone. Water intake was increased in TAC group, but addition of STGL decreased water intake volume. TAC treatment significantly increased area under the curve for glucose (AUCg) (TAC+S10: 459.2±25; TAC+S20: 392.7±33 vs. TAC: 534.7±25 mg/dL.min; $p<0.05$), but STGL co-treatment recovered these values compared with the TAC alone. Decreased serum insulin level by TAC treatment was significantly increased when combined with STGL20, 40 (TAC+S20:0.44±0.05; TAC+S40:0.44±0.03 vs.TAC:0.29±0.03 ng/mL; $p<0.05$). Islet size was significantly decreased in TAC group, but it was recovered when it combined with STGL40 (TAC+S40:5631.6±1384.6 vs. TAC: 3910.3±626.4 UM; $p<0.05$). Addition of STGL (10or20) on TAC was significantly reduced serum 8-OHdG level compared with TAC alone (TAC+S10: 0.40±0.22; TAC+S20:0.49±0.09vs. TAC:0.80±0.12 ng/mL $p<0.05$).

Conclusion: DPP-4 inhibitor has a protective effect on Tacrolimus-induced diabetes by decreasing TAC-induced oxidative stress.

Key Words: Tacrolimus, Sitagliptin, 췌장
Tacrolimus, Sitagliptin, Pancreas