

## Tacrolimus에 의한 당뇨에서 metformin의 투여가 미치는 효과

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### Discrepant Effect of Metformin on Hyperglycemia in Rats with Tacrolimus- or Sirolimus-induced Diabetes Mellitus

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**Background:** Metformin is a widely used drug in the treatment of immunosuppressant-induced hyperglycemia. Previously, we reported that combined treatment of metformin reduced sirolimus-induced blood glucose level. In this study, we aimed to investigate the effects of metformin in tacrolimus-induced hyperglycemia.

**Methods:** Four groups (n=12) of normal Sprague-Dawley rats were studied: animals received tacrolimus (1.5 mg/kg) and/or metformin (200 mg/kg) or vehicle for 4 weeks under the 0.05% salt diet. Body weight, water intake, and urine volume for 24 hr were measured before sacrifice. The effect of metformin on tacrolimus-induced hyperglycemia was evaluated by assessing intraperitoneal glucose tolerance test (IPGTT), histopathology, and serum insulin level. For further analysis, isolated rat beta cells from normal rats were treated with tacrolimus (30 ng/mL) and/or metformin (165 ng/mL) for 12 hr, then glucose-stimulated insulin secretion (GSIS) were performed.

**Results:** After four weeks, treatment with tacrolimus decreased body weight, and water intake and urine volume were increased compared with vehicle group. Treatment with tacrolimus caused elevated blood glucose level evaluated by IPGTT and reduced serum insulin level compared with vehicle. Islet size by measuring insulin-positive area was significantly decreased in tacrolimus-treated group. Combined treatment of metformin did not improved tacrolimus-induced diabetes. In vitro study for GSIS, tacrolimus and/or metformin-treated isolated islets showed a reduction in insulin secretion ability compared with tacrolimus alone.

**Conclusions:** In this study, we found that co-treatment of metformin may not confer to the insulin secretion capacity during tacrolimus treatment. Therefore, use of metformin should be considered in transplant recipients receiving tacrolimus.

**Key Words:** 이식, 타크로리무스, 메트포르민, 당뇨, 인슐린

Transplantation, Tacrolimus, Metformin, Diabetes mellitus, Insulin