

Sirolimus 단독투여 또는 cyclosporine과의 병합투여가 당뇨에 미치는 영향

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Effect of Sirolimus on Diabetes Mellitus in Rat with or without Cyclosporine Treatment with or without Cyclosporine Treatment

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Purpose : Combined treatment of sirolimus (SRL) and cyclosporine A (CsA) has synergistic nephrotoxicity, but the effect of SRL on CsA- induced pancreatic injury is unknown. We investigated the influence of SRL on pancreatic injury in rats with or without CsA treatment.

Methods : Sprague- Dawley rats maintained on a low salt diet (0.05% sodium) were treated subcutaneously with vehicle (olive oil, VH, 1mL/kg per day) and CsA (15 mg/kg per day) for 21 days. SRL (0.3 mg/kg per day) was concurrently administered via subcutaneously to CsA and VH groups. The effect of SRL on CsA- induced pancreatic injury was evaluated by intraperitoneal glucose tolerance test (IPGTT), plasma insulin concentrations, blood glucose level and pancreatic b- cell morphology.

Results : The VH+SRL group significantly increased blood glucose concentration, calculated AUC (806 ± 34 vs. 599 ± 13 mg/dL min, $p < 0.05$) and decreased plasma insulin concentration (0.37 ± 0.01 vs. 0.42 ± 0.01 ng/mL, $p < 0.05$) compared with the VH group. In the CsA group, blood glucose concentration and calculated AUC (1069 ± 49 mg/dL min, $p < 0.05$) significantly increased and plasma insulin concentration (0.33 ± 0.01 ng/mL, $p < 0.05$) was significantly lower than the VH and the VH+SRL group. Combined treatment of CsA and SRL group further increased blood glucose concentration and calculated AUC (1546 ± 38 vs. 1069 ± 49 mg/dL min, $p < 0.05$) and decreased the plasma insulin concentration (2.9 ± 0.02 vs. 0.33 ± 0.01 ng/dL, $p < 0.05$) compared with the CsA group. Immunohistochemical staining for insulin in the VH group and VH+SRL group showed strong and uniform pattern of the islet cells. In contrast, a lower intensity of insulin staining and vacuolization in islet cells were observed in the CsA group compared with the VH or the VH+SRL groups. Combined treatment of CsA+SRL group showed further increased the vacuolization in the pancreas islet cells and decreased pancreatic b islet mass.

Conclusion : Combination of sirolimus and CsA aggravates CsA- induced pancreatic injury.

Key Words : 사이클로스포린, 시롤리무스, 췌장
Cyclosporine A, sirolimus, Pancreas