

Cyclosporine에 의해 유도된 췌장손상 시 sirolimus로 대체 투여하였을 때 Srolimus가 당뇨에 미치는 영향

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Influence of Switch from Cyclosporine to Sirolimus in Pancreatic Injury Caused by Cyclosporine

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Purpose : Sirolimus (SRL) is a new drug with both immunosuppressant and anti-proliferative properties that has a unique mechanism of action distinct from that of the calcineurin inhibitor (CNI). However, it is not undetermined whether SRL can be replaced in CNI-induced diabetes mellitus (DM). We investigated the influence of switch from cyclosporine A (CsA) to SRL on established CsA-induced DM.

Methods : Sprague-Dawley rats were used, and four groups were included Vehicle (VH), switch from olive oil to SRL groups (VH/SRL), CsA withdrawal groups (CsAW) and switch from CsA to SRL groups (CsA/SRL). All rats maintained on a low salt diet (0.05% sodium) were treated subcutaneously with VH (olive oil, 1mL/kg per day) and CsA (15 mg/kg per day) for 28 days. And then SRL (0.3 mg/kg per day) was concurrently administered via subcutaneously to CsA and VH groups for 28 days. The effect of SRL on CsA-induced pancreatic injury after switch from CsA to SRL was evaluated by intraperitoneal glucose tolerance test (IPGTT), plasma insulin concentrations, blood glucose level and pancreatic β -cell morphology.

Results : Blood glucose concentration, calculated AUC and did not differ between VH and CsA withdrawal group. In VH/SRL groups, blood glucose concentration and calculated AUC (581 ± 37 vs. 484 ± 30 mg/dL min, $p < 0.05$) were increased compared with VH group (983 ± 46 vs. 484 ± 30 mg/dL min, $p < 0.05$). In the CsA/SRL group, blood glucose concentration and calculated AUC were further increased compared with the VH/SRL groups (983 ± 46 vs. 581 ± 37 mg/dL min, $p < 0.05$). Immunoreactivity of insulin in the CsA/SRL group was lower than other three groups. Plasma insulin level did not differ between VH and CsA withdrawal groups, but VH/SRL group showed significantly decreased plasma insulin concentration compared with the VH group (3.90 ± 0.27 vs. 4.38 ± 0.35 mg/dL min, $p < 0.05$). In CsA/SRL group, plasma insulin level was further decreased compared with the VH/SRL groups (3.70 ± 0.21 vs. 3.90 ± 0.27 mg/dL min, $p < 0.05$).

Conclusion : Switch from CsA to SRL dose not improve pancreatic injury caused by CsA.

Key Words : 사이클로스포린, 시롤리무스, 췌장
Cyclosporin A, Sirolimus, Pancreas