

Sirolimus 단독 치료가 야생형 생쥐 신장에 미치는 효과

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Effect of Isolated Sirolimus Treatment on Wild Type Mouse Kidneys

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Objectives: Sirolimus, a mammalian target of rapamycin inhibitor, is widely used in transplantation. However, several side effects of sirolimus such as proteinuria and edema remain unresolved and the precise mechanism is still unclear. To elucidate whether isolated sirolimus treatment induces proteinuria, we treated C57BL/6 mice with different doses of sirolimus.

Methods: Mice were injected intraperitoneally with 0, 3, 10 or 30 mg/kg/day of sirolimus for 24 days. Urinary albumin excretion was quantified by a double-sandwich enzyme-linked immunosorbent assay, and serum creatinine level was measured with a single dry-film chemistry auto-analyzer. The mRNA levels were measured by polymerase chain reaction.

Result: Urinary albumin was not detected in the sirolimus-treated mice. But, serum creatinine levels were increased in dose dependent manner and significantly higher in 30 mg/Kg sirolimus treated group than control. Glomerular mRNA expression profiling revealed decreased levels of the podocyte related genes (WT-1, synaptopodin, nephrin, CD2AP and podocin), and fibrosis maker TGF-beta in the sirolimus-treated mice. Furthermore, there were reduced anti-apoptotic genes Bcl-2 and Bcl-xL expression level.

Conclusion: Although sirolimus treatment showed decreased expression of slit diaphragm associated genes and elevated serum creatinine level, it failed to induce proteinuria in this model. Further studies are required to evaluate the condition in which sirolimus induces proteinuria.

Key Words: 시로리무스, 단백뇨, 족세포

Sirolimus, Proteinuria, Podocyte