

스트렙토조토신 유발 당뇨병성 신증에서 산화 및 염증 손상에 Sildenafil이 미치는 효과에 대한 연구

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Effects of Sildenafil on Oxidative and Inflammatory Injuries of the Kidney in Streptozotocin Induced Diabetic Rats

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Background : Oxidative and inflammatory injuries are implicated in the pathogenesis of nephropathy in diabetes. The aim of this study is to examine the effects of sildenafil (Viagra[®]), a type- 5 phosphodiesterase (PDE- 5) inhibitor, on diabetes- induced oxidative (iNOS, nitrotyrosine) and inflammatory (MCP- 1, ED- 1) injuries in the kidney of diabetic rats.

Methods : Diabetes mellitus (DM) was induced by a single injection of streptozotocin (STZ) in male Sprague Dawley rats. Diabetic rats were treated with sildenafil (50 mg/L in the drinking water) or not (simple dinking water) for 8 weeks and compared with age matched healthy controls. Systolic blood pressure, urinary albumin excretion rate, and serum creatinine were measured. Cortical mRNA levels of inducible nitric oxide synthase (iNOS), and monocyte chemotactic protein (MCP- 1) were measured by semiquantitative RT- PCR method. The expressions of iNOS, nitrotyrosine, and ED- 1 were determined by immunohistochemical staining.

Results : In sildenafil- treated diabetic rats, a kidney- to- body weight ratio was lower than that of sildenafil- untreated diabetic rats (9.8 ± 1.4 mg/g vs. 11.9 ± 0.3 mg/g; $p < 0.05$). Serum creatinine was not different among three groups. Urinary albumin excretion in diabetic rats was 378.0 ± 415.3 μ g/24hrs, which was significantly reduced after sildenafil treatment (79.5 ± 64.9 μ g/24hrs; $p < 0.05$) without significant change of systolic blood pressure. In sildenafil- treated diabetic rats, the expressions of iNOS and MCP- 1 in RT- PCR were lower than those of sildenafil- untreated diabetic rats ($p < 0.05$). In immunohistochemistry, the staining of iNOS, nitrotyrosine, and ED- 1 positive cells in renal tubules and glomeruli was more intense in sildenafil- untreated diabetic rats, as compared with that of control rats, which was significantly attenuated by sildenafil administration ($p < 0.05$).

Conclusion : This study shows that sildenafil treatment may attenuate the renal damage via the mechanism of inhibiting oxidative and inflammatory injuries in STZ- induced diabetic rats.

Key Words : Sildenafil, 산화, 염증

Sildenafil, Oxidative injury, Inflammatory injury