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백서의 cisplatin 신독성 모델에서 sildenafil의 신보호 효과

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Pretreatment of Sildenafil Attenuates Renal Injury in an Experimental Model of Rat Cisplatin-Induced Nephrotoxicity

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Introduction : Sildenafil (Viagra; Pfizer, New York, NY) is the first commercially available selective inhibitor of phosphodiesterase- 5 (PDE5) to be widely used for the treatment of erectile dysfunction. In recent years, there has been considerable interest in investigating the role of sildenafil in protection against injury of heart in animal models. We evaluated the protective effect of sildenafil against experimental Model of rat cisplatin- induced nephrotoxicity.

Methods : Male SD rats were divided into seven groups; control rats, sildenafil- contro rats (0.5 mg/kg, intraperitoneal (IP) dose, daily), L- NAME- control rats (15 mg/kg, intraperitoneal (IP) dose), cisplatin rats (5 mg/kg IP single dose) and Sildenafil- treated IR rats (0.5 mg/kg, daily). L- NAME- treated IR rats, and Sildenafil and L-NAME- treated IR rats. Renal gene expression levels of TNF- α , Fas, FasL, Bcl- 2, iNOS, eNOS and GAPDH were measured by real- time PCR 24 hrs after IR injury. Renal bcl- 2, EKR/pERK, and caspase- 3 activation was evaluated by western blot, We examined TUNEL, and light microscopic findings.

Results : Serum level of creatinine in etanercept treated IR rats 24 hrs after IR injury (2.34±0.76 mg/dL, M±SD) was significantly lower than that of untreated IR injured rats (3.47±0.67 mg/dL, M±SD) ($p<0.05$). Renal gene expression levels of TNF- α , Fas, FasL, and iNOS in untreated IR rats were significantly higher than those of Sham op rats. The levels of TNF- α , Fas, FasL, iNOS gene expressions of sildenafil treated IR rats were significantly lower than those of untreated IR rats (all, $p<0.01$). The Bcl- 2 gene expression level of sildenafil treated IR rats was significantly higher than that of untreated rats ($p<0.05$). Pretreatment of sildenafil in IR injured rats significantly reduced renal caspase- 3 activation ($p<0.01$) and TUNEL positive apoptotic cells ($p<0.01$), and significantly increased pErk and bcl- 2 protein.

Conclusion : In conclusion, the results of the present study suggest that sildenafil has a renal protective effect on experimental cispatin- induced renal injury and anti- apoptotic effect of sildenafil may be involved in this mechanism.

Key Words : 실데나필, cisplatin 신독성, 세포사멸
Sildenafil, Apoptosis, Cisplatin nephrotoxicity