F-B12

백서의 신허혈재관류 모델에서 Etanercept의 신보호 효과

충남대학교병원 내과[1], 가톨릭의대 대전성모병원 내과[2], 충남대학교병원 조직병리과[3]

최대은[1] · 나기량[1] · 장윤경[2] · 이상주[2] · 정사라[1] · 임범진[3] · 이강욱[1] · 김석영[2] · 신영태[1]

Pretreatment of TNF-α Blockade, Etanercept Attenuates Ischemia-Reperfusion Renal Injury

Dae Eun Choi[1], Ki Ryang Na[1], Yoon Kyung Chang[2], Sang Ju Lee[2], Sarah Chung[1]
Beom Jin Lim[3], Kang Wook Lee[1], Seok Young Kim[2] and Young Tai Shin[1]

Internal Medicine Chungnam National University[1], Internal Medicine Daejeon St. Mary[2]
Pathology Chungnam National University[3]

Introduction : TNF-α is known to mediate inflammation and apoptosis in ischemia- reperfusion (IR) injury of kidneys. Etanercept is a soluble TNF-α receptor with anti- inflammatory and anti- apoptotic effects in several animal renal injury models including chronic renal insufficiency and unilateral ureteral obstruction. We evaluated the protective effect of etanercept against experimental renal IR injury.

Methods : Male SD rats were divided into four groups; saline- control rats, etanercept- control rats (10 mg/kg, intraperitoneal (IP) dose), untreated IR rats (reperfusion 35 minutes after nephrectomy of right kidney with clamping of left renal artery and vein) and etanercept- treated IR rats (10mg/kg, single IP dose12 hours prior to IR injury). Renal gene expression levels of TNF-α, Bcl- 2, iNOS and MCP- 1 were measured by real- time PCR 24 hrs after IR injury. Renal caspase- 3 activation was evaluated by western blot and immunohistochemistry, The magnitude of apoptosis of renal tubular cells was determined by TUNEL assay.

Results : Serum level of creatinine in etanercept treated IR rats 24 hrs after IR injury (1.69±0.07 mg/dL, M±SD) was significantly lower than that of untreated IR injured rats (2.31±0.16 mg/dL, M SD) ($p<0.01$). Renal gene expression levels of TNF-α, MCP- 1 and iNOS in untreated IR rats were significantly higher than those of saline-control rats. The levels of MCP- 1 and iNOS gene expressions of etanercept treated IR rats were significantly lower than those of untreated IR rats (all, $p<0.01$). The Bcl- 2 gene expression level of etanercept treated IR rats was significantly higher than that of untreated rats ($p<0.05$). Pretreatment of etanercept in IR injured rats significantly reduced renal caspase- 3 activation ($p<0.01$) and TUNEL positive apoptotic cells ($p<0.01$).

Conclusion : In conclusion, the results of the present study suggest that TNF-α blockade, etanercept has a protective effect on experimental IR renal injury and at least in part, the anti- apoptotic effect may be involved in this mechanism.

Key Words : Etanercept, 허혈재관류손상, 세포사멸
Etanercept, Ischemia reperfusion injury, Apoptosis