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Cisplatin 신독성에 대한 Erythropoietin의 효과

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Renoprotective Effect of Erythropoietin on Experimental Cisplatin-induced Renal Injury

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Introduction : Erythropoietin (EPO) modulates a broad array of cellular processes that include progenitor stem cell development, cellular integrity, and angiogenesis. The results of recent studies show that systemically administered EPO is protective in vivo, in several animal models of renal injury including ischemia-reperfusion injury. Inflammation and oxidative stress are important events among the plethora of mechanisms involved in cisplatin-induced nephrotoxicity. The aim of this study was to evaluate the effect of EPO in the protection against cisplatin-induced renal dysfunction.

Methods : Male Spague-Dawley rats weighing 230-250 g were divided into four groups; untreated-control group, cisplatin-treated group (10 mg/kg body weight, single intraperitoneal dose), EPO-treated group (3,000 unit/kg body weight, intraperitoneal injection for 5 successive days) and the fourth group was treated with both drugs and EPO treatment was started 1 day prior to cisplatin administration. Five days after cisplatin administration all experimental groups were sacrificed. Competitive RT-PCR was performed for the estimation of TGF-beta, MCP-1, TNF-alpha, osteopontin, Fas and Bcl-2 gene expression levels of the kidneys. We also evaluated the magnitude of tubulointerstitial damage by semiquantitative tissue damage score on light microscopic examination.

Results : Serum level of creatinine of EPO treated cisplatin rats five days after cisplatin administration (1.5±0.7 mg/ dL, M±SE) was significantly lower than that of untreated cisplatin rats (5.1±1.5 mg/dL) ($p<0.01$). On microscopic examination, the magnitude of renal tubulointerstitial damage of EPO treated cisplatin rats was also significantly less than that of untreated cisplatin rats ($p<0.01$). Renal gene expressions of TGF-beta, TNF-alpha, osteopontin, MCP-1 and Fas in untreated cisplatin injected rats were significantly higher than those of untreated-control rats. The levels of TGF-beta, TNF-alpha, osteopontin and Fas gene expressions of EPO treated cisplatin rats were significantly lower than those of untreated cisplatin injected rats (all, $p<0.05$). The Bcl-2 mRNA level of EPO treated cisplatin rats was significantly higher than that of untreated cisplatin injected rats.

Conclusion : In conclusion, the results of the present study suggest that EPO has a renal protective effect on experimental cispatin-induced renal injury and at least in part, antiapoptotic effect of EPO may be involved in this mechanism.