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The Effect of Recombinant Human Erythropoietin in Experimental Gentamicin Induced Nephrotoxicity

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Background: Erythropoietin (EPO), originally identified for its critical role in promoting erythrocyte survival and differentiation, has been shown to exert multiple paracrine/autocrine functions. Protective effects of EPO have been demonstrated in various tissues and experimental methods of ischemia-induced injury. In the present study, we investigated the effect of EPO on an in vivo rat model of gentamicin-induced nephrotoxicity and the possible mechanism implicated in the EPO-mediated anti-apoptotic action.

Methods: Eighteen male Spraque-Dawley rats were divided into 4 groups. 1. Saline (S) group (n=4), 2. E group (n=4), was administrated EPO (3,000 IU/kg) intraperitoneally, 3. G group (n=5), was adminiSae Yong Hongstrated gentamicin (80 mg/kg) intraperitoneally, 4. EG group (n=5), was administrated gentamicin (80 mg/kg) with EPO (3,000 IU/kg) intraperitoneally for 7 days. After 8 days of the first gentamicin injection, renal dysfunction and injury was assessed by measurement of serum biochemical markers (BUN, creatinine) and histological grading. RT-PCRs for the gene expression levels of TGF-β, MCP-1, Bcl-2, Fas in the kidney and immunoblotting for ERK and caspase-3 were performed.

Results: BUN and serum creatinine in the G group, administrated gentamicin, were significantly higher than that of the S group, and in the EG group, administrated gentamicin with EPO, were significantly lower than that of the G group ($p<0.05$). The extent of tubular necrosis of the EG group was significantly smaller than that of the G group ($p<0.001$). The renal mRNA expression of TGF-β, MCP-1, Fas were decreased in the EG group as compared with those of the G group. Bcl-2 expression was increased in the EG group as compared with that of the G group. p-ERK expression was increased in the EG group as compared with that of the G group. But caspase-3 expression was decreased in the EG group as compared with that of the G group.

Conclusion: The present study demonstrated that EPO attenuates renal injury in gentamicin-induced rat models. The cytoprotective action of EPO against gentamicin-induced nephrotoxicity seems to be associated with its anti-apoptotic action.

Key Words: 에리스로포이에틴, 젠타마이신, 신독성
Erythropoietin, Gentamicin, Nephrotoxicity