

Renoprotective Effect of rHEPO in Experimental Gentamicin Toxicity

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Purpose : Recently EPO has been proved to be cytoprotective in various renal injury models, ischemic-reperfusion, cisplatin nephrotoxicity, obstructive nephropathy by ureteral obstruction, through its antiapoptotic action in cell signaling pathways. In this study, we try to prove the renoprotective effect of recombinant human EPO in gentamicin, representative aminoglycoside notorious for its nephrotoxicity, induced proximal tubular damage also through its antiapoptotic action like other renal injury models.

Methods : There were 4 groups in this study. Saline group (S, n=6), EPO group (E, n=6), Gentamicin group (GM, n=6), Group preconditioning with EPO 3 days before gentamicin injection followed by concomitant injection of EPO and gentamicin for subsequent 7 days (EPO+GM, n=6). The dose of gentamicin that induced nephrotoxicity in experimental rats is 100 mg/kg/day intraperitoneally. Preconditioning and maintenance doses of EPO were 3,000 U/kg/day intraperitoneally. Degrees of renal insufficiency were evaluated by measuring BUN and serum creatinine in blood samples at sacrifice and by calculating histologic scores (the percentage of necrotic proximal tubule area in light microscopic inspection fields).

Results : Checked BUN level were 10.02 ± 0.84 mg/dL, 12.5 ± 1.49 mg/dL, 86.3 ± 30.8 mg/dL, 38.2 ± 26.1 mg/dL in S group, E group, GM group, EPO+GM group respectively. Checked serum creatinine level were 0.50 ± 0.03 mg/dL, 0.55 ± 0.04 mg/dL, 4.11 ± 1.28 mg/dL, 1.44 ± 0.74 mg/dL, respectively. There were increases of BUN, serum creatinine levels in GM group compared with S, E groups significantly ($p < 0.001$), but decreased in EPO+GM group significantly ($p < 0.05$). Necrotic tubule area percentages calculated from light microscopic findings were $39.3 \pm 13.3\%$ in GM group, $14.03 \pm 7.54\%$ in EPO+GM groups and it means that necrotic proximal tubule areas was reduced significantly by preconditioning with EPO ($p < 0.001$).

Conclusion : rHEPO is renoprotective in nephrotoxicity induced by gentamicin.