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Inhibition of gentamicin–induced renal tubular cell necrosis

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ABSTRACT

Gentamicin nephrotoxicity limit its usage against gram negative bacteria. Most researches showed that antioxidant agents improved gentamicin nephrotoxicity. According to these investigations oxidative stress play a central role in the mechanism of gentamicin induced nephrotoxicity. Recently Rafieian-Kopaei and colleagues showed that erythropoietin significantly ameliorated serum creatinine, blood urea nitrogen and tubal necrosis in gentamicin induced nephrotoxicity in rat. One of the advantages of this study is treatment of rats for 10 days by erythropoietin after inducing gentamicin nephrotoxicity and besides co- treatment of gentamicin and erythropoietin at 10 days simultaneously. They showed that erythropoietin improved significantly serum creatinine and blood urea nitrogen in gentamicin injected rats simultaneously and even after gentamicin nephrotoxicity induction. This study also showed that erythropoietin ameliorates histopathological injuries especially tubular cell necrosis that induced by gentamicin. Although the detailed renoprotective mechanisms of erythropoietin cannot be fully explained by this study but histological and biochemical results are satisfactory.

Commentary

Implication for health policy/practice/research/medical education:
Most researches against gentamicin nephrotoxicity focused on the use of various antioxidants. In the recent study Rafieian-Kopaei et al. investigate the effect of erythropoietin in inhibition of gentamicin nephrotoxicity. They showed that erythropoietin improved significantly serum creatinine , blood urea nitrogen and histopathological injuries especially tubular cell necrosis in gentamicin injected rats simultaneously and even after gentamicin nephrotoxicity induction. Although the detailed renoprotective mechanisms of erythropoietin cannot be fully explained by this study but histological and biochemical results are satisfactory.

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Amino nucleoside antibiotic gentamicin sulphate is commonly used for the treatment of Gram-negative bacterial infection, but nephrotoxicity side effects limit its use. In spite of undesirable gentamicin nephrotoxicity, this antibiotic still constitute the only effective therapeutic alternative against microorganisms - pseudomonas, proteus and serratia - insensitive to other antibiotics (1). Moreover, gentamicin has been widely used as a model to study of acute

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renal failure in experimental animals.

The mechanisms of gentamicine nephrotoxicity are not completely known. However the pathological mechanisms involved in gentamicin induced nephrotoxicity include induction of oxidative stress, apoptosis, necrosis, up regulation of transforming growth factor B, elevation of endothelin I , increase of monocyte/macrophages infiltration , phospholipidosis an increase of intracellular sodium ions (2,3). Gentamicin has been showed to increase the generation of super oxide anions, hydroxyl radicals, hydrogen peroxide and reactive nitrogen species in kidney and lead to renal injuries (1).Gentamicin induced renal damage is linked with lipid peroxidation and protein oxidation in renal cortex. In other hand, gentamicin reduces efficiency in kidney antioxidant enzymes like superoxide dismutase, catalase, glutathione proxidase and glutathione (2).

Gentamicin nephrotoxicity is characterized functionally by an increase of serum creatinine, blood urea nitrogen, and decrease in glomerular filtration rate (4), which morphologically characterized by proximal tubule epithelial desquamation, tubular necrosis, tubular fibrosis, epithelial edema and glomerular hypertrophy (5).

Most researches against gentamicin nephrotoxicity focused on the use of various antioxidants. It may be said that the central role of gentamicin nephrotoxicity is oxidative stress and inflammation: a loop of damage amplification and a connection between mechanisms of tubular and glomerular changes (3).

More investigations showed that antioxidant agents satisfactory inhibited or attenuated gentamicin renal toxicity in rats. Usage of antioxidants improved serum creatinine, blood urea nitrogen, creatinine clearance and histological injuries such as tubular necrosis, tubular cell edema and apoptosis in gentamicin injected rats (6, 7). In the recent study, Rafieian-Kopaei and colleagues investigated the effect of erythropoietin in inhibition of gentamicin nephrotoxicity (8). Although erythropoietin acts as hemopoietic factor but this hormone show abilities such as anti inflammation, anti apoptosis (9), malondialdehyde lowering and increasing of catalase activity (10).One of the advantages of Rafieian-kopaei et al. study is treatment of rats for 10 days by erythropoietin after inducing gentamicin nephrotoxicity and besides co-treatment of gentamicin and erythropoietin at 10 days simultaneously.Rafieian-Kopaei and colleagues showed that erythropoietin improved significantly serum creatinine and blood urea nitrogen in gentamicin injected rats simultaneously and even after gentamicin nephrotoxicity induction. This study also showed that erythropoietin ameliorates histopathological injuries especially tubular cell necrosis that induced by gentamicin .Moreover use of erythropoietin after gentamicin nephrotoxicity revealed that erythropoietin induced tubular cell regeneration by unknown mechanism. Although the detailed renoprotective mechanisms of erythropoietin cannot be fully explained by this study but histological and biochemical results are satisfactory.

Conflict of interest

The author declared no competing interests.

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