Antioxidants for Prevention of Gentamicin-induced Nephrotoxicity

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Acute kidney injury (AKI) mainly develops following ischemic or toxic insults and is characterized by acute tubular injury and kidney dysfunction.[1-3] However, pathogenesis of AKI is complex, and promoting events may be completely different, but similar pathways may be implicated in subsequent injury responses.[4-8] To study AKI models, various methods were defined for each specific condition. Gentamicin, derived from gram-positive bacteria, has potential in treating aerobic gram-negative bacteria. Gentamicin has been extensively used for inducing AKI in experimental animals and evaluation of kidney protective agents, too. Accumulation of gentamicin in renal proximal tubule cells may trigger renal toxicity, which leads to brush border network injury.[9,11] The renal toxicity involves kidneys free radical production and accretion, utilization of antioxidant defense mechanisms, and acute renal tubular cells necrosis,[9-12] which leads to diminished glomerular filtration rate and kidney dysfunction. The pathological mechanisms also involve rise of endothelin-1, upregulation of transforming growth factor-, augmentation of oxidative stress, significant increase in monocyte/macrophage infiltration into the renal cortex and medulla, apoptosis, and also necrosis.[10-15] Gentamicin has also been shown to amplify the generation of superoxide anions, hydrogen peroxide, hydroxyl radicals, and reactive nitrogen species in the proximal tubular cells and lead to kidney damage.[9,10]

Most researchers on gentamicin kidney toxicity therefore focused on the use of various antioxidants.[9,10] Indeed, the role of renal mitochondria on protection against gentamicin kidney toxicity, the role of antioxidants in either protecting or mitigating gentamicin renal toxicity and integrative glomerular and tubular effects and their possible interplay had been described. Thus, it should be noted again that gentamicin administration can induce severe renal toxicity. Therefore, the modalities to protect against gentamicin-induced AKI can apply to the other conditions or agents that act mainly through the generation of reactive oxygen species in the kidney. In fact, AKI is a common clinical entity with high mortality and morbidity rates.[8-11] A large number of patients who also have other morbidities such as diabetes mellitus, vascular disease, or chronic kidney diseases are at a high risk to develop AKI due to ischemic and nephrotoxic insults.[11-15] In these conditions, it is possible that calcium dobesilate, which is shown to have antioxidant efficacy, is capable of protecting the renal tubular cells against injurious insults. Calcium dobesilate is a strong antioxidant and is safe.[16] Various studies have shown that calcium dobesilate acts as a free radicals scavenger; thus, as reported by Jafary and colleagues in the current issue of the *Iranian Journal of Kidney Diseases*,[16] it is possible to use it for prevention of renal tubular cell injury.[16,17] However, more clinical studies are suggested to fully define its role as kidney protecting agent.

CONFLICT OF INTEREST

None declared.

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What is the Real Risk Factor of Urinary Calculi in Iranian Children?

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The earliest reports on urolithiasis in Iranian children in 1980s revealed calcium oxalate and ammonium acid urate were the most common components of urinary calculi.[1-3] Since then there have been increasing numbers of published studies about the risk factors of urolithiasis in Iranian children. A cross-sectional study conducted by Akhavan and coworkers[4] showed the incidence of urinary calculi in school-aged children in Qom was 1% . They simultaneously studied the urinary excretion of metabolic factors in those school-aged children. Surprisingly, 23% of asymptomatic children without calculus showed hypercalciuria and all of them had hypocitraturia.[4] The result should be interpreted cautiously because of potential technical error, different normal ranges for Iranian children, or nutritional factors.

Alamzadeh-Ansari and colleagues studied 152 infants with microlithiasis and urolithiasis by collecting 24-hour urine samples in south-west of Iran.[5] In their report published in this issue of the *Iranian Journal of Kidney Diseases*, they detected that 92% had metabolic disorder, family history of urinary calculi was positive in 67%, and at least one-third of parents had consanguinity marriage. Similarly, the most metabolic disorders in this study were hypercalciuria and hypocitraturia. They mentioned neither the rate of mixed metabolic disorders nor the other risk factors such as dehydration, low fluid intake, and the diet of