Comment on: A model for prediction of cisplatin induced nephrotoxicity by kidney weight in experimental rats

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Cisplatin (cis-diamminedichloroplatinum II), as one of the most applicable and potent anticancer medication, is used in the treatment of a various pediatric and adult malignancies. However, it gives side-effects such as renal toxicity which is dose-dependent, and thus limited its usage. Treatment with cisplatin induces the inflammatory mechanisms, which leads to a reduction in the antioxidant levels, leading to a failure of the antioxidant protection against free-radical damage generated by antitumor drugs. The oxidative stress, induced by cisplatin in the kidney was partially inhibited by antioxidant therapy using selenium, glutathione, flavonoids, and superoxide dismutase.

Key words: Cisplatin, kidney, nephrotoxicity

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Cisplatin (cis-diamminedichloroplatinum II), as one of the most applicable and potent anticancer medication, is used in the treatment of a various pediatric and adult malignancies. However, it gives side-effects such as renal toxicity which is dose-dependent, and thus limited its usage. Treatment with cisplatin induces the inflammatory mechanisms, which leads to a reduction in the antioxidant levels, leading to a failure of the antioxidant protection against free-radical damage generated by antitumor drugs. The oxidative stress, induced by cisplatin in the kidney was partially inhibited by antioxidant therapy using selenium, glutathione, flavonoids, and superoxide dismutase. Therefore various agents, containing herbal and chemical drugs have been tested to find their efficacy to reduce cisplatin-induced nephrotoxicity. The renal toxicity effects of cisplatin are demonstrated by a decrease in creatinine clearance and electrolyte disturbances, mainly hypomagnesemia, largely due to the acute cytotoxic effects of cisplatin on distal and proximal tubules. There were two points that should be remembered from the study of Ashrafi, et al. Firstly, in recent years much attention has been directed towards the gender difference in cisplatin renal toxicity. Indeed, there are sharp sex-dependent differences in reaction rates and the probability of side effects in individuals treated with chemotherapy. Gender-biased expression levels of metabolic enzymes and transporters in kidney directing to different pharmacokinetics have been explained for most common anticancer drugs. It was found that in female gender drug half-life is often longer, which is associated with improved survival, but also increased toxicity. Secondly, in the study conducted by Ashrafi et al., normalized kidney weight and morphological damage scores has been proposed to be is an acceptable predictor of kidney function in cisplatin-induced renal toxicity in experimental rats. However, a variety of novel urinary biomarkers have been recognized and partially qualified for use as the markers for kidney damage in rats with acute kidney injury. These novel biomarkers are lipocalin-2, glutathione S-transferase-yb1 (GSTYb1), osteopontin, renal papillary antigen 1 (RPA-1) and urinary albumin, alpha glutathione s-transferase (α-GST), kidney injury molecule-1 (KIM-1), and plasma cystatin C; alongside the traditional biomarkers of plasma creatinine, urea, urinary total protein, glucose, and n-acetyl-beta-d-glucosaminidase (NAG). Hence in the near future, some of these urinary biomarkers may be suggested to more precisely show the cisplatin kidney toxicity and accepted as the biomarkers of cisplatin renal injury. It should be pointed out that, investigations regarding gender difference in cisplatin renal injury is scarce and more investigations needs to find the clinical significance of gender on renal injury induced by cisplatin. Also, more
study on the biomarkers of acute kidney injury during cisplatin toxicity suggests to better find the acute kidney injury of cisplatin and effectively abolishes damages to the kidneys and decrease morbidity of these patients.[4,5,9-12]

REFERENCES


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