Re: Effect of Alcoholic Extract of Nigella Sativa on Cisplatin-induced Toxicity in Rat

IJKD 2013;7:165-7
www.ijkd.org

Dear Editor,

We read with interest the recently published article in the *Iranian Journal of Kidney Diseases*, by Hadjzadeh and colleagues, entitled "Effect of alcoholic extract of Nigella sativa on cisplatin-induced toxicity in rat.[1]" The study has focused on reduction of cisplatin-induced nephrotoxicity by *Nigella sativa* (NS) seeds on 30 rats, in an experimental study. They found that NS seeds had nonsignificant effects on biochemical parameters. While the histopathologic properties of the kidneys relatively recovered after using NS. The authors should be applauded for their efforts on finding a way to reduce cisplatin-induced nephrotoxicity (CIN). However, beside this work, we would like to mention a few points about CIN.

In a preclinical study to find the protective effects of endogenous nitric oxide donor (L-arginine) from CIN, we studied 33 Wistar rats and we found that L-arginine had protective effects against CIN in the male rats; however, it promotes the induced damage in female rats. We described a gender-related difference in rat model of CIN.[2] Moreover, ameliorative effects of vitamin E were evaluated in another study on 32 Wistar rats.[3] We also showed the nephroprotective effects of losartan as an angiotensin II receptor 1 blockade in CIN in Wistar rats.[3] In another study, surprisingly, we found that low doses of magnesium supplementation, intensified kidney toxicity and kidney dysfunction in CIN in the rat model. We concluded that the protective role of magnesium with moderate and high doses is not certain.[4] We also observed that co-administration of vitamin C and losartan was not more effective than the administration of vitamin C or losartan alone.[5,6]

Although the role of gender in CIN is not well known, we recently conducted a study on rat model of CIN and observed that losartan may prevent CIN in male rats, but it promotes the cisplatin -induced damage in female rats, which may be related to the renin-angiotensin system receptors in the kidneys.[7] Additionally, we recently reported that, vitamin E, vitamin C, and losartan have no ameliorative effects against CIN in the presence of estrogen in ovariectomized rats,[8] which is in agreement with our previous findings. More recently, we also observed that estrogen abolishes protective effect of erythropoietin against CIN in ovariectomized rats,[9] while renoprotective effects of erythropoietin were also showed in our previous studies.[10-12] Hence, it is well documented that there is a gender difference in the CIN in the rat model. It is documented that some cases of chronic kidney diseases are gender-related too.[13-16] Few studies published regarding sex difference in CIN. Therefore, there still remains a number of big questions to further explore mechanisms interact in CIN. In this regard, to better understanding the factor of gender difference in CIN, more experimental rat model and clinical studies are suggested.

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Re: Effect of Renin-Angiotensin-Aldosterone System Blockade Therapy on Incidence of Contrast-induced Nephropathy in Patients With Chronic Kidney Disease

Dear Editor,

We read the article "Effect of Renin-Angiotensin-Aldosterone System(RAAS) Blockade Therapy on Incidence of Contrast-induced Nephropathy in Patients with Chronic Kidney Disease" by Spatz et al with interest.[1] They investigated the possible impact of use of the renin-angiotensin-aldosterone system medications on the incidence of contrast-induced nephropathy (CIN) in patients with mild-to-moderate chronic kidney disease who received coronary angiography. They suggested that patients on angiotensin-converting enzyme inhibitors or angiotensin receptor blockers while undergoing cardiac catheterization are not at a higher risk of developing CIN. Prospective randomized trials are needed to help determine the effect of RAAS blockade on CIN.

Contrast-induced nephropathy is the leading cause of hospital-acquired renal failure. The CIN causes prolonged hospitalization, increased cost and incidence of renal and cardiovascular events, and mortality. The elderly patients have more risk of CIN because of decreased renal reserve and the other factors. These factors, including an estimated glomerular filtration rate (GFR) less than 60 mL/min/1.73 m^2, left ventricular ejection fraction less than 45%, diabetes mellitus, hypotension, anemia, age over 70 years, emergency percutaneous coronary intervention (PCI), a history of myocardial infarction, and contrast agents dose higher than 200 mL, were identified as risk factors for CIN after PCI.[2] On the other hand, hyperlipidemia, smoking, and alcohol consumption may be associated with CIN.[3] In the present study, information about patient charecteristics such as arterial blood pressure level of before contrast exposure, anemia, hyperlipidemia, emergency PCI, history of myocardial infarction, smoking, and alcohol consumption was not defined. It would be better if the authors had provided infomation about these factors.

In addition, even mild chronic kidney dysfunction, as a GFR less than 90 mL/min, and dehydration are a risk factor of CIN in previous studies.[4] On