Response to "Nephrotoxicity: Evidence in Patients Receiving Cisplatin Therapy"

Mehdi Nematbakhsh, PhD

An article by Duffy, Fitzgerald, Boyle, and Rohatgi (2018) was published in the April issue of the *Clinical Journal of Oncology Nursing*. Based on review, the authors suggested some clinical recommendations to protect the kidneys against cisplatin-induced nephrotoxicity, including hydration or supplementation of magnesium or mannitol during cisplatin administration. In addition to clinical findings, the related basic sciences data may be helpful in formulating treatment guidelines in cisplatin therapy. This letter will present several suggestions for future clinical studies based on laboratory findings.

Cisplatin-induced nephrotoxicity has been reported to be gender related (Aydin, Agilli, & Aydin, 2014; Nematbakhsh et al., 2013, 2017; Pezeshki, Maleki, Talebi, & Nematbakhsh, 2017; Pinches et al., 2012), and risk for nephrotoxicity is higher in men than in women. The kidney function marker is also altered by cisplatin (Stakisaitis et al., 2010). The ability of supplementations to attenuate cisplatin-induced nephrotoxicity was also gender related (Eshraghi-Jazi et al., 2011; Haghighi et al., 2012; Naseem, Hassan, Alhazza, & Chibber, 2015; Zamani et al., 2016). The female sex hormone estrogen was found to aggravate cisplatin-induced nephrotoxicity (Ghasemi et al., 2016; Nematbakhsh et al., 2012, 2013). Hypomagnesemia is a well-known side effect of cisplatin, and magnesium supplementation was suggested by Duffy et al. (2018); however, the protective role of magnesium against cisplatin-induced nephrotoxicity has failed in the laboratory (Ashrafi et al., 2012; Soltani, Nematbakhsh, Eshraghi-Jazi, Talebi, & Ashrafi, 2013). Beta cell dysfunction is a metabolic disorder that may also alter the effect of cisplatin-induced nephrotoxicity. In another study, streptozotocin-induced diabetic rats were protected against cisplatin-induced nephrotoxicity (Soltani et al., 2013).

These laboratory findings should not be minimized. Clinical trials are needed to find the role of gender, sex hormones, and accompanying disease in cisplatin-induced nephrotoxicity. Looking at more factors will certainly help reduce the side effects of the drug and will be beneficial to patients whose only hope of life may be the beneficial effects of the drug in their cancer treatment.

Mehdi Nematbakhsh, PhD, is a professor of physiology in the Water and Electrolytes Research Center and Department of Physiology at the Isfahan University of Medical Sciences in Iran. Nematbakhsh can be reached at nematbakhsh@med.mui.ac.ir, with copy to CJONEditor@ons.org.

No financial relationships to disclose.

REFERENCES

Ashrafi, F., Haghshenas, S., Nematbakhsh, M., Nasri, H., Talebi, A., Eshraghi-Jazi, F., . . . Safari, T. (2012). The role of magnesium supplementation in cisplatin-induced nephrotoxicity in a rat model: No nephroprotectant effect. *International Journal of Preventive Medicine, 3,* 637–643.

Aydin, I., Agilli, M., & Aydin, F.N. (2014). Gender differences influence renal injury in cisplatin-treated rats: Biochemical evaluation. *Biological Trace Element Research, 158,* 275.

Duffy, E.A., Fitzgerald, W., Boyle, K., & Rohatgi, R. (2018). Nephrotoxicity: Evidence in patients receiving cisplatin therapy. *Clinical Journal of Oncology Nursing, 22,* 175–183. https://doi.org/10.1188/18.CJON.175-183

Eshraghi-Jazi, F., Nematbakhsh, M., Nasri, H., Talebi, A., Haghighi, M., Pezeshki, Z., . . . Ashrafi, F. (2011). The protective role of endogenous nitric oxide donor (L-arginine) in cisplatin-induced nephrotoxicity: Gender related differences in rat model. *Journal of Research in the Medical Sciences, 16,* 1389–1396.

Ghasemi, M., Nematbakhsh, M., Pezeshki, Z., Soltani, N., Moeini, M., & Talebi, A. (2016). Nephroprotective effect of estrogen and progesterone combination on cisplatin-induced nephrotoxicity in ovariectomized female rats. *Indian Journal of Nephrology, 26,* 167–175. https://doi.org/10.4103/0971-4065.160337

Haghighi, M., Nematbakhsh, M., Talebi, A., Nasri, H., Ashrafi, F., Roshanaei, K., . . . Safari, T. (2012). The role of angiotensin II receptor 1 (AT1) blockade in cisplatin-induced nephrotoxicity in rats: Gender-related differences. *Renal Failure, 34,* 1046–1051. https://doi.org/10.3109/0886022X.2012.700886

Naseem, I., Hassan, I., Alhazza, I.M., & Chibber, S. (2015). Protective effect of riboflavin on cisplatin induced toxicities: A gender-dependent study. *Journal of Trace Elements in Medicine and Biology, 29,* 303–314. https://doi.org/10.1016/j.jtemb.2014.08.003

Nematbakhsh, M., Ebrahimian, S., Tooyserkani, M., Eshraghi-Jazi, F., Talebi, A., & Ashrafi, F. (2013). Gender difference in cisplatin-induced nephrotoxicity in a rat model: Greater intensity of damage in male than female. *Nephro-Urology Monthly, 5,* 818–821. https://doi.org/10.5812/numonthly.10128

Nematbakhsh, M., Pezeshki, Z., Eshraghi-Jazi, F., Ashrafi, F., Nasri, H., Talebi, A., . . . Mansouri, A. (2012). Vitamin E, vitamin C, or losartan is not nephroprotectant against cisplatin-induced nephrotoxicity in presence of estrogen in ovariectomized rat model. *International Journal of Nephrology, 2012,* 284896.