Journal of Preventive Epidemiology

http jprevepi.com

Antioxidant therapy to improve cisplatin nephrotoxicity

Niloufar Hooshyar[1], Banafsheh Yalameha[2], Mehrnoosh Sedighi[3], Mohammadreza Khosravifarsani[4*], Parto Nasri[5]

[1]Faculty of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran
[2]Department of Biochemistry, Faculty of Medicine, Lorestan University of Medical Sciences, Khorramabad, Iran
[3]Cardiovascular Research Center, Shahid Rahimi Hospital, Lorestan University of Medical Sciences, Khoramabad, Iran
[4]Cancer Prevention Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
[5]Infectious Diseases and Tropical Medicine Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

Correspondence to:
Mohammadreza Khosravifarsani,
Email:
drmohammadkhf@gmail.com

Received: 21 April 2019
Accepted: 10 May 2019
ePublished: 4 June 2019

Citation: Hooshyar N, Yalameha B, Sedighi M, Khosravifarsani M, Nasri P. Antioxidant therapy to improve cisplatin nephrotoxicity. J Prev Epidemiol. 2019;4(1):e08.

Core tip

Considering the substantial role of antioxidants in the reduction of cisplatin nephrotoxicity, it is suggested that antioxidant therapy can be an innovative approach to improve cisplatin nephrotoxicity

Cisplatin (CDDP) as one of the main anticancer drugs is widely applied in the treatment of various types of cancers such as lung, head, neck, ovary, breast, and testis. Despite the antineoplastic property of cisplatin, several side effects have been reported for this synthetic drug including gastrotoxicity, ototoxicity, neurotoxicity, allergic reactions, myelosuppression and also nephrotoxicity (1,2). Nephrotoxicity due to cisplatin is a key problem which is related to the administration of this drug via the accumulation in the tubular epithelial cells. The mitochondrial and DNA nuclear damage and generation of reactive oxygen species (ROS) resulted in cisplatin administration that can induce inflammatory responses and the activation of apoptosis and necrosis pathways. The ROS generation especially hydroxyl radicals are accepted as the main consequence of cisplatin nephrotoxicity that stimulates protein oxidation, lipid peroxidation, and DNA damage (3, 4).

Recently, evidence has been demonstrated the therapeutic role of different antioxidants in amelioration of cisplatin nephrotoxicity such as superoxide dismutase, catalase, selenium, vitamin E and C, N-acetylcysteine, L-arginine, lycopene, cannabidiol, and others (5-7). N-acetylcysteine (NAC) is a thiolate compound, mucus decomposer and a potent antioxidant compound which can be effective in cancer, cardiovascular disease, hepatotoxicity, and metal toxicity. Intravenous administration of NAC is more effective than oral and intraperitoneal administration of this agent to reduce the complications of cisplatin. A study showed that NAC is more effective with lower doses for renoprotection (8). Furthermore, vitamin E is widely considered to be a lucrative antioxidant in cisplatin nephrotoxicity. In fact, the beneficial effects of vitamin E on cisplatin nephrotoxicity are probably due to several factors such as antioxidant, anti-inflammatory, immunoregulatory, and anti-apoptotic properties. The strong antioxidant effects of vitamin E have been confirmed in various studies, including an animal model of cisplatin-induced nephrotoxicity (CIN) previously (9). It has been indicated that cisplatin-induced kidney damage is reduced by administration of the nitric oxide (NO) precursor molecule (10). A study revealed that intravenous injection of L-arginine at 260-263 mg/kg alongside the administration of cisplatin at 6 mg/kg, plasma urea and creatinine levels decreased significantly in the groups receiving L-arginine. The administration of L-arginine decreased polyurea and increased inulin clearance. L-arginine is a source of NO production and as an inhibitor of N-nitro l-arginine methyl ester (L-NAME) production. Additionally, L-arginine reduces oxidative stress and subsequently CIN (11). Therefore, considering the substantial role of antioxidants in the reduction of cisplatin nephrotoxicity, it is suggested that

antioxidant therapy can be an innovative approach to solve this problem.

Authors' contribution
All authors wrote the manuscript equally.

Conflicts of interest
The authors declare no conflict of interest.

Ethical considerations
Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

Funding/Support
None.

References
1. Hartmann JT, Lipp HP. Toxicity of platinum compounds. Expert Opin Pharmacother. 2003; 4:889-901.
2. Sastry J, Kellie SJ. Severe neurotoxicity, ototoxicity and nephrotoxicity following high-dose cisplatin and amifostine. Pediatr Hematol Oncol. 2005; 22:441-5.
3. Ashrafi F, Nematbakhsh M, Safari T, Talebi A, Nasri H, Khazaei M, et al. A combination of vitamin C and losartan for cisplatin-induced nephrotoxicity in rats. Iran J Kidney Dis. 2012; 6:361-5.
4. Karasawa T, Steyger PS. An integrated view of cisplatin-induced nephrotoxicity and ototoxicity. Toxicol Lett. 2015; 237:219-27. doi: 10.1016/j.toxlet.2015.06.012.
5. Miller RP, Tadagavadi RK, Ramesh G, Reeves WB. Mechanisms of Cisplatin nephrotoxicity. Toxins (Basel). 2010; 2:2490-518. doi: 10.3390/toxins2112490.
6. Naziroglu M, Karaoğlu A, Aksoy AO. Selenium and high dose vitamin E administration protects cisplatin-induced oxidative damage to renal, liver and lens tissues in rats. Toxicology. 2004; 195:221-30.
7. Atessahin A, Yilmaz S, Karahan I, Ceribasi AO, Karaoglu A. Effects of lycopene against cisplatin-induced nephrotoxicity and oxidative stress in rats. Toxicology. 2005; 212:116-23.
8. Dickey DT, Muldoon LL, Doolittle ND, Peterson DR, Kraemer DF, Neuwelt EA. Effect of N-acetylcysteine route of administration on chemoprotection against cisplatin-induced toxicity in rat models. Cancer Chemother Pharmacol. 2008; 62:235-41 doi: 10.1007/s00280-007-0597-2.
9. Marquardt D, Williams JA, Kučerka N, Atkinson J, Wassall SR, Katsaras J, et al. Tocopherol activity correlates with its location in a membrane: a new perspective on the antioxidant vitamin E. J Am Chem Soc. 2013;22;135:7523-33. doi: 10.1021/ja312665r.
10. Cylwik D, Mogielnicki A ,Buczko Wo. L-arginine and cardiovascular system. Pharmacol Rep. 2005;57:14-22.
11. Saleh S, El-Demerdash E. Protective effects of L-arginine against cisplatin-induced renal oxidative stress and toxicity: role of nitric oxide. Basic Clin Pharmacol Toxicol. 2005; 97:91-7. doi: 10.1111/j.1742-7843.2005.pto_114.x.