Antioxidant therapy to improve cisplatin nephrotoxicity

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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
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References