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Effect of high fat diet feeding on cisplatin-induced nephrotoxicity in mice

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Objectives:

Nephrotoxicity of cisplatin limits its use in the cancer therapy. Cisplatin injected is excreted through kidney. During this excretion cisplatin is accumulated in the mitochondria of kidney tubule cells and disrupts the structure and function of mitochondria. This cisplatin toxicity is associated with mitochondrial oxidative stress. Since an over-providing of nutrients affects cellular redox balance, in this study, we investigated the role of high-fat diet intake in cisplatin-induced nephrotoxicity.

Methods: C57BL/6 male mice were administered with either cisplatin (20 mg/kg B.W.) or saline. Some mice were fed high-fat diet (HFD) for 7 days before cisplatin injection. Renal function and damage were evaluated by blood urea nitrogen (BUN) concentration and PAS staining. Oxidative stress and mitochondrial damages were determined.

Results: Cisplatin injection caused the disruption of kidney tubular cells and increase of BUN. These increases were greater in HFD-fed mice than normal diet (ND)-fed mice. Levels of 4-HNE expression and DNA oxidation increased in the kidney after cisplatin injection and these increases were also greater in the HFD-fed mice than ND-fed mice. Mitochondrial damage after cisplatin injection was more severe in the HFD-fed mice than ND-fed mice. Interestingly HFD feeding significantly increased the level of peroxisome proliferator-activated receptor-gamma coactivator-1α (PGC-1α), a member of a family of transcription coactivators, in the kidneys when compared with ND feeding. Cisplatin injection decreased PGC-1α in both HFD and ND, representing greater decrease in the HFD-fed mice. Cisplatin decreased opa1 in the kidney along with a greater decrease in the HFD-fed mice than ND-fed mice. In contrast, cisplatin increased fis1 expression in the kidney, and this increase was greater in the kidney of HFD-fed mice than ND-fed mice.

Conclusions:

These results indicate that high-fat diet worsens cisplatin-induced nephrotoxicity along with a greater mitochondrial damage and oxidative stress, suggesting that. Cisplatin nephrotoxicity may be controlled by food supply.