KSN 2019
Seoul, Korea · May 23 - 26

Abstract Type : Poster
Abstract Submission No. : PO-1199

The effect of diet on cisplatin-induced nephrotoxicity

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Objectives: The use of cis-diamminedichloroplatinum (II) (cisplatin), an effective chemotherapeutic agent, is limited by its side effects including nephrotoxicity. Cisplatin nephrotoxicity is associated with the increase of reactive oxygen species (ROS). Starvation and over providing of food affect cellular redox balance through the regulation of ROS producing and removing systems. Therefore, in this study, we investigated whether starvation and high-fat diet feeding affect cisplatin nephrotoxicity, and if so, its mechanisms.

Methods: C57BL/6 male mice were administered with either cisplatin (20 mg/kg B.W.) or saline. Before those administrated mice were fed a normal diet, starved for 2 days, given high-fat diet feeding for 7 days, or starved for 2 days and then given normal diet for 2 days. Renal function was evaluated by plasma creatinine (PCr) and BUN concentration. Kidney damage was evaluated by PAS staining. Protein expression, ROS production, and oxidative stress were determined in the kidneys.

Results: Cisplatin induced kidney tubule disruption and functional impairment. BUN and PCr levels were highest in the high-fat diet feeding mice and lowest in the starved mice in positive correlation with kidney damage. In addition, hydrogen peroxide formation and oxidation of DNA in the kidney after cisplatin were in a similar order with BUN, PCr and kidney injury. After cisplatin injection, mitochondrial oxidative stress and damage were highest in high-fat diet mice, while lowest in starved mice after cisplatin injection. In contrast, the expression of PGC-1α, a key regulator of mitochondria biogenesis, was lower in high-fat diet mice than in starvation and normal diet mice after cisplatin injection.

Conclusions: Data indicate that high-fat diet worsens cisplatin-induced nephrotoxicity along with increased oxidative stress and mitochondria fission, whereas starvation attenuates those. These results suggest that energy metabolism is critically associated with cisplatin nephrotoxicity and cisplatin nephrotoxicity may be controlled by food supply.