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Ceria-Zirconia nanoparticles as an enhanced antioxidant attenuates apoptosis of human kidney proximal tubular epithelial cells in hypoxia

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Objectives: Hypoxia is an important cause of acute kidney injury (AKI) in various conditions because kidneys are one of the most susceptible organ to hypoxia. Reactive oxygen species (ROS) play an important role in hypoxia induced AKI by affecting the function of cellular DNA, proteins, and lipids. The use of antioxidants can benefit the control and prevention of hypoxia induced AKI. Ceria-Zirconia nanoparticles (CZ NPs) exhibit superoxide dismutase and catalase mimetic activities. . We investigated the effect of CZ NPs in cultures of hypoxia exposed human proximal tubular epithelial cells.

Methods: CZ NPs with size 2-3nm were synthesized using non-hydrolytic sol-gel reaction. To investigate the catalytic effect of CZ NPs, reactive oxygen species (ROS) production was measured using DHE, DCF-DA and amplex red assay. Cellular survival rate and cytotoxicity were measured with 3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyl tetrazolium bromide (MTT) assay. Cellular signaling pathway were studied by real time polymerase chain reaction and Western blot analysis. Mitochondria ROS were measured with Mitosox. Mitochondrial function, dynamics and number were measured with seahorse XFe96 analyzer, mitotracker staining and Western blot analysis (OPA1, DRP1, cytochrome c)

Results: Cell survival was reduced in a dose-dependent manner for 24h after hypoxia exposure. Hypoxia caused a significant increase in ROS production 24 h after hypoxia. The extent of the effect of hypoxia on ROS levels was significantly reduced by CZ NPs treatment in not only cytoplasm but also mitochondria. CZ NPs downregulated proinflammatory markers and reduced caspase 3/7 activity in hypoxic HK-2 cells. The number of mitochondria was recovered and the fission of mitochondria reduced after CZ NPs exposure in hypoxia.

Conclusions: CZ NPs have the potential as a therapeutic medicine for preventing ROS-related hypoxia induced AKI by attenuating mitochondrial damage.