Prophylactic treatment with antioxidant nanoparticles attenuate ischemia/reperfusion injury in BALB/c mice

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Background: Ischemia/reperfusion (I/R) injury is one of the important cause of delayed graft function, graft rejection and chronic graft dysfunction. Ceria nanoparticle is known that exhibit free radical scavenger and catalytic activities. When zirconia attached to ceria nanoparticles, the ceria atom tend to remain Ce^{3+} and the efficacy as a free radical scavenger increase. We studied whether ceria and ceria-zirconia nanoparticles (CZ NPs) as an antioxidant are effective to protect I/R injury in kidneys.

Methods: BALB/c mice were randomized into four groups: group 1 (control, normal saline pretreatment plus sham operation; n=6), group 2 (CZ NPs pretreatment plus sham operation; n=6), group 3 (normal saline pretreatment plus I/R; n=6) and group 4 (CZ NPs pretreatment plus I/R; n=6).

Results: The levels of plasma blood urea nitrogen (BUN) and creatinine of group 3 (I/R operation) were significantly increased when compared to group 1 (control, sham operation). However, in group 4 (CZ NPs plus I/R operation), the plasma levels of BUN and creatinine were significantly decreased when compared to group 3 (I/R operation). In Hematoxylin and Eosin staining for analyzing histologic changes there was no significant difference between group 1 and group 2, but tubular dilatation, cellular casts, loss of tubular brush borders, vacuolar degeneration and tubular epithelial cell shedding were observed in group 3. In group 4, tubular damage was restored when compared to group 3. To detect apoptotic changes in kidney cells, terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) assay was done. In group 3, there was a significant number of positive cells in the TUNEL staining, whereas in group 4, the number of TUNEL positive cells was significantly decreased.

Conclusions: Collectively, CZ NPs were successfully uptaken into kidney cells and effectively attenuated I/R induced acute kidney injury in vivo, suggesting that could be a novel approach to control I/R injury induced graft injury.

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