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Alpha-lipoic Acid Attenuates Lipopolisaccharide-induced Kidney Injury

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Background: Kidney is one of the major target organs in sepsis, while effective prevention of septic acute kidney injury (AKI) has not yet been established. Alpha-lipoic acid (ALA) has been known to exert beneficial effects against lipopolysaccharide (LPS)-induced damages in various organs, such as heart, lung, and liver, but not in kidney. We investigated the protective effect of ALA on LPS-induced kidney injury.
Methods: Two groups of rats were treated with LPS (20 mg/kg, i.p.), one of which being cotreated with ALA (50 mg/kg). The control group was treated with vehicle only. Human renal proximal tubular epithelial cells (HK-2 cells) were cultured with LPS (10 μg/ml) in the absence or presence of ALA (210 μg/ml) for 3 hours prior to LPS treatment.
Results: Plasma creatinine level was increased in LPS treated rats, which was attenuated by ALA co-treatment. Terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) positive cells increased in the kidneys of LPS treated rats compared with controls, which was counteracted by ALA treatment. 4',6-diamidino-2-phenylindole (DAPI) staining also revealed nuclear fragmentation, condensation and shrinkage and heavy staining in HK-2 cells treated with LPS, which was prevented by ALA. LPS treatment induced cleaved caspase-3, inducible nitric oxide synthase (iNOS), aquaporin (AQP) 2 expression, which were counteracted by ALA in immunoblotting of reanl cortex and outer stripe of outer medulla. Increased protein expression of phospho-extracellular signal-regulated kinases 1/2 and c-Jun N-terminal kinases by LPS treatment was attenuated by ALA pretreatment, while p38 was not affected by either LPS or ALA treatment in HK-2 cells. Immunohistochemical staining demonstrated the expression of cyclooxygenase-2 and iNOS was enhanced, while that of AQP 1 was decreased in the kidneys from LPS rats, which was attenuated by ALA cotreatment
Conclusion: ALA treatment attenuates LPS-induced kidney injury by suppression of apoptosis, inflammation, and renal tubular dysfunction.

Key Words: Alpha-lipoic acid, Apoptosis, Inflammation, Kidney, Lipopolysaccharide