

백서 시스플라틴 신손상 모델에서 α -Lipoic acid의 신보호 효과의 기전

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α -Lipoic Acid Attenuates Cisplatin-Induced Tubulointerstitial Injury by Inhibition of Mitochondrial Bax Translocation In Rats

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Introductions : Recent studies have demonstrated that apoptosis, a programmed cell death characterized by DNA fragmentation, as well as necrosis might play a central role in the pathogenesis of AKI. Representative pathways of apoptotic signaling cascade were clarified in a few studies; intrinsic mitochondrial pathway, extrinsic death receptor pathway and endoplasmic reticulum stress related mechanism. Among those pathways, Bax activation through intrinsic mitochondrial pathway, a separate way from extrinsic death-receptor pathway, has also been mainly incriminated in cisplatin nephrotoxicity in vitro . We hypothesized that α -lipoic acid (LA) may attenuate cisplatin induced nephrotoxicity through inhibition of mitochondrial Bax expression in vivo.

Methods : Rats were treated with cisplatin (6 mg/kg) with or without pretreatment of LA (100 mg/kg×3 times). Renal function was evaluated using BUN, serum creatinine, and fractional excretion of sodium. Morphological changes were observed by light microscopy, TUNEL assay and degrees of damage were scored respectively. Western blottings for Bax, cytochrome c, caspase- 3, caspase- 9 were investigated.

Results : LA pretreated group significantly decreased both BUN and serum creatinine as compared to cisplatin group. Morphologically, both tubulointerstitial damages and apoptosis of tubular cells decreased significantly by LA pretreatment as compared to cisplatin group. LA pretreatment blocked the translocation of mitochondrial Bax, reduced the release of cytochrome c, decreased the expression of caspase- 3 and caspase- 9. as compared to cisplatin group.

Conclusion : Our results show that LA effectively attenuates cisplatin- induced tubulointerstitial damages in vivo by inhibition of mitochondrial Bax translocation.

Key Words : Bax protein, alpha- Lipoic acid