

MnTMPyP, MnSOD Mimetic, Inhibits Ischemia/reperfusion-induced Renal Fibrogenesis in Mice

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Renal ischemia/reperfusion (I/R) injury induces oxidative stress through producing excessive free radicals, and gradually progresses fibrosis. Role of oxidative stress in I/R- induced progression of renal fibrosis remains to be defined. Here, we examined the post- ischemic changes of oxidative stress and antioxidant enzymes, and the effect of manganese(III) tetrakis(1- methyl- 4- pyridyl)porphyrin (MnTMPyP), a mimetic of manganese superoxide dismutase (MnSOD) on I/R- induced renal fibrosis. Thirty min of bilateral ischemia followed by 16 days of reperfusion induced collagen deposition, tubular atrophy and the accumulation of infiltrated cells and increases of α - smooth muscle actin (α - SMA) and proliferating cell nuclear antigen (PCNA) expression in kidneys. Significant increases of hydrogen peroxide production and lipid peroxidation, whereas significant reduction of catalase, copper- zinc superoxide dismutase (CuZnSOD) and MnSOD activities were observed the post- ischemic kidney tissues. Administration of MnTMPyP from 3 days after the reperfusion daily for 14 days significantly mitigated post- ischemic decreases of catalase, CuZnSOD and MnSOD activities, showing the reductions of tissue hydrogen peroxide levels and lipid peroxidation. The administration of MnTMPyP significantly reduced post- ischemic increases of collagen deposition, tubular atrophy, interstitium expansion, and α - SMA and PCNA expression. These results demonstrate that I/R- induced renal fibrosis is associated with oxidative stress and reduction of oxidative stress reduces renal fibrosis- induced transient renal ischemia.

Key Words : 허혈/재관류, 섬유화, MnSOD
Ischemia/reperfusion, Fibrosis, MnSOD