S-B4

빌리루빈이 산화 스트레스와 세포 자멸사를 감소시킴으로서 신 세뇨관 손상을 호전시키는가

을지병원 내과[1], 분당서울대병원 내과[2]

오세원[1], 성수아[1], 이소영[1], 이은성[2], 안신영[2], 김세중[2], 나기영[2], 채동완[2], 진호준[2]

Bilirubin Attenuates the Renal Tubular Injury by Inhibition of Oxidative Stress and Apoptosis

Se Won Oh[1], Su Ah Sung[1], So Young Lee[1], Eun Seong Lee[2], Shin Young Ahn[2]
Sejoong Kim[2], Ki Young Na[2], Dong Wan Chae[2], Ho Jun Chin[2]

Department of Internal Medicine[1] Eulji General Hospital Eulji University College of Medicine
Department of Internal Medicine[2] Seoul National University Bundang Hospital Seoul National University

Background: Bilirubin (BIL) has been recognized as an endogenous antioxidant that shows a protective effect for cardiorenal diseases. We investigated whether administration of BIL had a protective effect on cyclosporine (CsA)-induced nephropathy (CIN), and examined the effects of BIL on the oxidative stress and apoptosis.

Methods: BIL was pretreated intraperitoneally three times for a week (60mg/kg), and CsA was injected for 4 weeks (15 mg/kg/day, subcutaneous). Proximal tubular epithelial (HK2) cells were pretreated with 0.1mg/ml of BIL for 24 hours, and then treated with 20 □M of CsA for another 24 hours.

Results: CsA induced marked increases in urine kidney injury molecule-1 (Kim-1) and neutrophil gelatinase-associated lipocalin (NGAL) concentrations ($p<0.05$). BIL reduced urine Kim-1 in CIN ($p<0.05$), while urine NGAL exhibited a decreasing tendency. In CsA-treated rat kidneys, the protein expression of NOX4 and p22phox was reduced by BIL ($p<0.05$). BIL ameliorated CsA-induced arteriolopathy, tubulointerstitial fibrosis, tubular injury, and the apoptosis examined by TUNEL assay ($p<0.01$). In HK2 cells, BIL reduced intracellular reactive oxygen species in CsA-treated cells. CsA increased the protein expression of bax, cleaved caspase-9, caspase-3 and the activity of caspase-3; however, the anti-apoptotic bcl-2 protein was reduced. These changes were recovered by BIL ($p<0.05$).

Conclusion: The direct administration of BIL protected against CsA-induced tubular injury via inhibition of oxidative stress and apoptosis.

Key Words: 세포자멸사, 빌리루민, 산화 스트레스
Apoptosis, Bilirubin, Oxidative stress