S-C13

당뇨병성 신증의 동물 모델에서 Bis 단백의 항산화 역할에 대한 연구

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정성진, 임지희, 김민영, 양근석, 홍유아, 신석준, 김형욱, 김용수, 장윤식, 박철휘

Role of Bis as an Antioxidant Protein in Diabetic Nephropathy

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Introduction: Bcl-2 interacting cell death suppressor (Bis) is ubiquitously expressed in various tissues and exhibits anti-stress and anti-apoptotic activity. Recently, it has been shown that suppression of Bis expression causes cells to become more susceptible to oxidative stress. Notably, oxidative stress-induced apoptosis contributes the pathogenesis of diabetic nephropathy. In this study, we investigated the potential role of Bis as an antioxidant protein in diabetic nephropathy.

Methods: We induced diabetic nephropathy in the mice with heterozygous genotype for bis gene (Bis-HT) and compared the resulting phenotypes with wild type (Bis-WT) mice up to 20 weeks after diabetes induction.

Results: Renal injuries represented by decrease in plasma creatinine and increase in albuminuria were aggravated in diabetic Bis-HT (Bis-HT DM) mice compared to diabetic Bis-WT (Bis-WT DM) mice. Moreover, the glomerular matrix expansion, TGF-beta1 and HIF-1alpha expression, and tubulointerstitial fibrosis were also notably increased in the Bis-HT DM mice than Bis-WT DM mice with the same degree of hyperglycemia. This severe outcome of diabetic nephropathy may be related to the increase in the proportion of apoptotic glomerular and tubular epithelial cells in Bis-HT DM mice. In addition, there was a decrease in Bis expression in Bis-HT DM mice as well as SOD1 and SOD2 expression, accompanied by an increase in oxidative stress. Furthermore, the treatment of an antioxidant tempol for 8 weeks starting after 12 weeks of diabetes induction reversed renal damage and the oxidative stress in Bis-HT DM mice. Bis-knockdown in mesangial cells decreased SOD1 and SOD2 expressions and induced oxidative stress.

Conclusion: Our results suggest that the decrease in antioxidant capacity of Bis may be a cause of the aggravation for nephropathy in Bis-HT DM mice.

Key Words: 당뇨병성 신증, 산화스트레스, 항산화제
Bis, Diabetic Nephropathy, Oxidative stress