Glycative stress and glyoxalase in kidney disease and aging

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The overwhelming glycation is referred to as “glycative stress”. Pathophysiological significance of glycative stress is emphasized in not only diabetic nephropathy but also kidney diseases related to hypoxic or oxidative stress. In particular, renal ischemia/reperfusion injury in the rats caused the tubular damages associated with glycative stress. The increase in tubular glycative stress by ischemia/reperfusion was associated with the decrease in glycation inhibitory enzyme, glyoxalase 1 (GLO1) in the kidney. Of note, ischemia/reperfusion-induced tubular damages were markedly ameliorated in GLO1 overexpressing rats. GLO1 transgenic rats also showed the retardation of renal senescence, especially tubular cell senescence, in association with age-induced interstitial thickening via lowering of glycative stress as well as oxidative stress. In addition, age-related aortic endothelial dysfunction (impairment of vasorelaxation, decrease in nitric oxide (NO) bioavailability, or inactivation of endothelial NO synthase (eNOS)) was ameliorated by suppression of glycative and oxidative stresses by GLO1. These evidences emphasized that modulation of glycative stress state enhances the tubular and endothelial homeostasis and resistance to not only tubular pathogens but also kidney aging. GLO1 might be a good target to develop anti-glycative stress drugs.

In conclusion, glycative stress links to hypoxia and oxidative stress and is a crucial pathogenic factor leading to various kidney diseases. The beneficial effect of GLO1 on lowering glycative stress might highlight the possibility of maintenance of kidney homeostasis.