[gw22-e0582]

AGING RELATED GLOMERULOSCLEROSIS IS ASSOCIATED WITH DECREASED IN KLOTHO EXPRESSION AND INCREASED IN SUPEROXIDE PRODUCTION

Zuo Zhong[1], Lei Han[1], Sun Zhongjie[2]1The First Affiliated Hospital of Chongqing Medical University, Chongqing, China; 2University of Oklahoma Health Sciences Center, Oklahoma, USA

10.1136/heartjnl-2011-300867.55

Objective Aging is associated with glomerulosclerosis and a decline in renal function. Klotho is a recently-discovered anti-aging gene. The purpose of this study was to determine changes in klotho, endothelin (ET) receptors, and superoxide production in kidneys of aged rats.

Methods Twenty Fisher 344xBrown Norway (F1) rats (male, 27 months) were divided into an Old Impaired group (n=9) and an Old Intact group (n=11) according to a cognitive function test. A group of 12-month-old rats (n=10) were used as a Young Intact group. Blood was collected for measuring serum creatinine and ET-1 concentration. Renal histology was evaluated using PAS staining and trichrome staining. The in situ superoxide production was measured in kidneys using dihydroethidium staining. Klotho protein, ET receptors, Nox2, interleukin-6 (IL-6), and MnSOD expression in renal cortex and medulla were assessed by immunohistochemistry and western-blotting.

Results Plasma creatinine was increased significantly in the Old Impaired group (2.32±0.20 mg/dl vs 1.18±0.12 mg/dl $p<0.01$), suggesting impaired renal function. Aged rats showed glomerulosclerosis and tubulointerstitial fibrosis. The glomerulosclerosis score and collagen area fraction were significantly higher in old impaired group than those in old intact, (3.34±0.26 vs 2.02±0.15, $p<0.01$); (5.62±0.36% vs 3.76±0.29% $p<0.05$), and they were significantly higher than those in young intact group (1.01±0.09, $p<0.05$, $p<0.01$); (2.42±0.16%, $p<0.05$, $p<0.001$). These pathological changes were markedly aggravated in the old cognitively impaired than in the old cognitively intact animals. Notably, aged rats demonstrated a significant decrease in klotho protein expression in renal cortex and medulla. Protein expression of IL-6, Nox2, ETA receptors and superoxide production were increased whereas MnSOD and ETB receptors expression were decreased in kidneys of the aged rats. Interestingly, these changes were more pronounced in the old impaired than in the old intact rats.

Conclusions The aging-related kidney damage paralleled with the cognitive function impairment. The aging-related glomerulosclerosis was associated with down regulation of klotho, ETB, and MnSOD expression but upregulation of ETA, IL-6, and Nox2 expression and superoxide production. These findings raise the necessity to further assess the roles of these factors and their relationship in aging-related kidney damage.