

Nrf2 activator, Resveratrol, Ameliorates Aging-related Progressive Renal Injury

Eun Nim Kim, Ji Hee Lim, Min Young Kim, Byung Ha Chung, Cheol Whee Park
Chul Woo Yang, Yong-Soo Kim, Yoon Sik Chang, Bum Soon Choi

Department of Internal Medicine, College of Medicine, The Catholic University of Korea

Background: The senescence markers of kidney have been shown to causes many changes in the energy metabolism. Two important issues in aging kidney are mitochondria dysfunction and oxidative stress. Nrf2 activator, Resveratrol is known to be useful in various diseases, For example, anti-cancer, anti-aging, anti-inflammatory, such as the effect of life has been reported, which may prevent inflammation and oxidative stress by activating SIRT1 and Nrf2. We examined that Resveratrol can potentially ameliorates the cellular condition, such as renal injury due to cell oxidative stress and mitochondria dysfunction caused by aging.

Methods: Male 19-month-old C57/BL6 mice were used in this study. Resveratrol (0.04%) was provided to old mice for 6 month. We compared histological change, oxidative stress, and aging-related protein expression in the kidneys between Resveratrol treated old-mice group (RSV) and vehicle old-mice group (VH).

Results: In our study, expression of Nrf2 in nuclear (1 ± 0.1 fold vs. 2 ± 0.4 fold) was increased in RSV. Expression of SIRT1 (1 ± 0.2 fold vs. 1.31 ± 0.11 fold) was increased in RSV. p-AMPK/Total AMPK ratio expression (1 ± 0.1 fold vs. 1.79 ± 0.2 fold) was increased in RSV compared with VH. RSV group displayed decreased albuminuria (46.5 ± 1.8 ng/24hr vs. 29.4 ± 2.0 ng/24hr) and Creatinine clearance (0.09 ± 0.006 ml/min vs. 0.26 ± 0.01 ml/min) increased with RSV. There were decreases in mesangial volume ($53.3\pm 1.6\%$ vs. $35.9\pm 1.4\%$), tubulointerstitial fibrosis ($10.1\pm 3.3\%$ vs. $4.8\pm 5.5\%$) and collagen IV ($16.6\pm 3.9\%$ vs. $8.4\pm 3.8\%$) in RSV. Immunohistochemistry of F4/80 expression in glomerulus ($1.9\pm 0.8\%$ vs. $0.4\pm 0.7\%$) and tubule ($1.1\pm 2.5\%$ vs. $0.2\pm 0.2\%$) were decreased in RSV compared with VH. Also, TGF- β ($0.6\pm 0.3\%$ vs. $0.4\pm 0.3\%$) was decreased in RSV. Urine isoprostane (21 ± 0.7 ng/24hr vs. 12.2 ± 0.7 ng/24hr) and 8-OHdG (74.3 ± 3.5 ng/24hr vs. 44.7 ± 4.6 ng/24hr) excretion decreased with aging. Antioxidant enzyme, such as SOD1 (1 ± 0.1 fold vs. 1.4 ± 0.3 fold), SOD2 (1 ± 0.2 fold vs. 1.3 ± 0.4 fold), HO-1 (1 ± 0.08 fold vs. 1.6 ± 0.1 fold) and NQO-1 (1 ± 0.06 fold vs. 1.3 ± 0.1 fold) were increased in RSV compared with VH.

Conclusions: These results suggest that activation of Nrf2 may benefit aging-related renal injury related with SIRT1 and AMPK activation by reducing oxidative stress. Pharmacologically targeting Nrf2 signaling molecules may reduce the pathologic changes of aging in the kidney.

Key Words: Aging, Kidney, Nrf2, SIRT1