The PPAR-α agonist, fenofibrate, ameliorates aging-related progressive renal injury

Introduction and Aims: Aging is a multifactorial process characterized by a progressive decline in physiological function. Peroxisome proliferator-activated receptor-α (PPAR-α) is key regulators in various age-associated physiological processes related to energy metabolism and oxidative stress. We therefore examined the activation of PPAR-α by PPARα agonists fenofibrate would improve changes of aging and oxidative stress in the kidney.

Methods: 19-month-old C57BL/6 mice were used in this study. Fenofibrate (0.1%) was provided to old mice for 6 months. We measured histological change, oxidative stress, and aging-related protein expression in the kidneys.

Results: Fenofibrate-treated old-mice displayed decreased albuminuria (59.4 ± 31 ng/24 hr vs. 22.7 ± 8.5 ng/24 hr; p < 0.05 vs. VH). Creatinine clearance increased with Fenofibrate-treated old-mice (0.07 ± 0.04 ml/min vs. 0.16 ± 0.05 ml/min; p < 0.05 vs. VH). Serum creatinine was decreased in Fenofibrate-treated old-mice, although this was not statistically significant (0.75 ± 0.3 mg/dL vs. 0.44 ± 0.2 mg/dL). There were decreases in mesangial volume (56.1 ± 2.06% vs. 42.87 ± 1.25%; p < 0.001 vs. VH) and tubulointerstitial fibrosis (16.1 ± 4.32% vs. 4.41 ± 3.61%; p < 0.001 vs. VH) in Fenofibrate-treated old-mice. In our study, expression of PPARα (1 ± 0.2 fold vs. 1.31 ± 0.11 fold; p < 0.05 vs. VH) was increased in Fenofibrate-treated old-mice. SIRT1 expression (1 ± 0.2 fold vs. 1.97 ± 0.23 fold; p < 0.05 vs. VH) was increased in Fenofibrate-treated old-mice compared with control-old mice. Also, expression of PGC-1α (1 ± 0.07 fold vs. 1.85 ± 0.13 fold; p < 0.05 vs. VH) was increased in Fenofibrate-treated old-mice.

Conclusions: These results suggest that PPAR-α agonists may benefit aging-related renal injury by SIRT1 activation. Pharmacologically targeting PPAR-α and SIRT1 signaling molecules may reduce the pathologic changes of aging in the kidney.