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자연발생 고혈압 쥐에서 고지방식이로 유발된 신장 손상 및 고혈압에 대한 tempol 혹은 candesartan의 효과

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Tempol or Candesartan Prevents High-Fat Diet-Induced Hypertension and Renal Damage in Spontaneously Hypertensive Rats

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Background : To date, the intrarenal mechanism whereby obesity induces and aggravates hypertension and renal disease remains poorly understood. Therefore, we investigated that the role of intrarenal oxidative stress or renin-angiotensin system (RAS) in diet-induced hypertension and renal inflammation in SHR fed a high-fat diet.

Methods : Male SHR and Wistar-Kyoto rats (WKY) at eight weeks of age were fed either a normal-fat diet or a high-fat diet without/ with tempol or candesartan treatment for 12 weeks.

Results : At the end of week 12, the high-fat fed SHR gained more body weight and periepididymal fat weight, had their systolic blood pressure further elevated, and had induced glucose intolerance. The high-fat diet resulted in increases in immunohistochemical stains of renin and angiotensin II with elevation of urinary TTKG and a decrease in natriuresis. The real-time PCR demonstrated significant increases in mRNA levels of renin, angiotensin and angiotensin converting enzyme in the kidney, reflecting enhanced activation of the intrarenal RAS, which was also shown by Western blot analysis. The expression of ED-1, osteopontin and TGF-β1 in the renal cortex were prominently enhanced in the high-fat fed SHR with increased intrarenal lipid concentrations and oxidative stress. Administration of tempol or candesartan in the high-fat fed SHR inhibited the elevation of the systolic blood pressure, intrarenal lipid concentrations, oxidative stress, the degree of renal inflammation, and the intrarenal RAS activity.

Conclusion : our findings suggest that high-fat diet-induced obesity aggravates hypertension and induces renal injury in SHR via intrarenal lipotoxicity, which results in enhancement of oxidative stress and the renin-angiotensin system in the kidneys. Inhibition of intrarenal oxidative stress and the renin-angiotensin system by a superoxide dismutase mimetic or angiotensin receptor blocker might have a therapeutic role in obesity-induced lipotoxicity, hypertension and renal inflammation.

Key Words : 고혈압, 비만, Renin-angiotensin syste
Hypertension, Obesity, Renin-angiotensin system