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아포지단백 E 제거 백서에서 장기적인 Deoxycorticosterone acetate 투여가 미치는 영향에 관한 연구

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Treatment of Deoxycorticosterone Acetate (DOCA)-salt Induces Proteinuria in Apolipoprotein E Knockout (ApoE) Mice

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Background : Deficiency of apolipoprotein E is considered to be related with poor prognosis of renal function in various diseases such as diabetes and transplant kidney, however, its mechanism is not clear. Moreover, it is known that angiotensin II accelerates the development of atherosclerosis in ApoE mice, but, the role of aldosterone in this process is unknown. So, we aimed to investigate the change of renal function and its mechanism in ApoE mice, and examine the effect of aldosterone by mineralocorticoid receptor stimulation.

Methods : C57bBL/6 (wild type) and ApoE mice which were received unilateral nephrectomy on 10 weeks were divided into 4 groups according to treatment with 1% NaCl or deoxycorticosterone acetate (DOCA)- salt in tap water (n=12/group). After 12 weeks, they were all sacrificed.

Results : All groups didn't show any differences in blood pressure and heart rate irrespective the treatment of DOCA, but urinary K excretion and aldosterone synthase gene activity were increased in DOCA treatment group, which means DOCA treatment stimulate aldosterone activity. Total cholesterol, triglyceride, and LDL cholesterol were higher in ApoE group. ApoE mice treated with DOCA- salt showed increase of urinary protein excretion not only compared to wild type, but also to ApoE mice treated with 1% NaCl. On histologic examination, mesangial expansion with cellular infiltration was noticed on glomerulus of Apo E mice, and it was aggravated with DOCA treatment. Angiotensin II receptor type 2 (AT2) expressions showed similar patterns with cellular infiltration. ApoE mice showed higher CD68 expression and lower adenosine triphosphate binding cassette A- 1 (ABCA1) and carnitine palmitoyl transferase (CPT- 1) activities compared to other groups, and they also showed more significant changes in DOCA treatment group.

Conclusion : ApoE mice might have changes in glomerulus such as cellular infiltration with increase of AT2 expression even before functional derangement. DOCA treatment, which resulted in increase of aldosterone activity, induced more aggravation of those changes of glomerulus and resulted in proteinuria in ApoE mice. They were associated with cellular lipid accumulation as a consequence of decrease of cholesterol efflux and increase of triglyceride synthesis.

Key Words : 아포지단백 E, 알도스테론, 단백뇨
Apolipoprotein E, DOCA, Aldosterone