

Early Treatment with Enalapril Is Not Renoprotective in 'Programmed' Obese 3 Month-old Rats

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Background: Countering the renin angiotensin system (RAS) has been reported to be beneficial in obese patients with chronic kidney disease. We have shown that early postnatal overnutrition leads to the development of renal injury in adult rats. This study was aimed to investigate that the RAS block in early life can ameliorate renal injury induced by early postnatal overnutrition.

Methods: Three or 10 male pups per mother were assigned to either the small litter (Obese group) or normal litter (Lean group) rats during the first 21 days of life. With this, all pups were randomized into 4 groups, and treated with enalapril (Obese enalapril, OE; Lean enalapril, LE) or vehicle (Obese control, OC; Lean control, LC) between the ages of 2 and 4 weeks postnatally. Body weight, blood pressure (BP) and renal alterations were determined at 3 months.

Results: Pups in the OC group weighed more than rats in the LC group between 7 days and 3 months of age ($p < 0.05$). Enalapril decreased body weights in the Lean group at weaning (22 days) and at 3 months ($p < 0.05$); however, body weights in the OE group were not different from the OC group at 3 months. Mean BP levels in the LE, OC and OE groups were higher than the LC group at 3 months ($p < 0.05$) while there was no difference between the OC and OE groups. At 3 months, the LE group showed increased renal cell apoptosis, glomerulosclerosis, and tubulointerstitial fibrosis and decreased renal cell proliferation, compared to the LC group ($p < 0.05$). The index scores of glomerulosclerosis and tubulointerstitial fibrosis were higher in the OE group than the OC group ($p < 0.05$). In immunoblotting and immunohistochemistry, the LE group showed increased intra-renal angiotensin II receptor type (AT) 2 and matrix metalloproteinase (MMP)-9 and decreased renin and tissue inhibitor of MMP (TIMP)-1 expression, compared to the LC group ($p < 0.05$). The OE group also demonstrated increased intra-renal AT2 and decreased AT1 and TIMP-1 expression, compared to the OC group ($p < 0.05$).

Conclusion: The RAS block in early life can induce the detrimental renal impact and may be not renoprotective in 'programmed' obese adult rats.

Key Words: 안지오텐신 II, 성장과 발달, 과영양

Angiotensin II, Growth and development, Overnutrition