Inhibidor da ECA mais ativador do VDR – efeito na glomerulosclerose, proteinúria e estresse oxidativo renal - murino

**Effect of combining an ACE inhibitor and a VDR activator on glomerulosclerosis, proteinuria, and renal oxidative stress in uremic rats.**


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**Abstract**

Angiotensin-converting enzyme (ACE) inhibitors ameliorate the progression of renal disease. In combination with vitamin D receptor activators, they provide additional benefits. In the present study, uremic (U) rats were treated as follows: U+vehicle (UC), U+enalapril (UE; 25 mg/l in drinking water), U+paricalcitol (UP; 0.8 μg/kg ip, 3 × wk), or U+enalapril+paricalcitol (UEP). Despite hypertension in UP rats, proteinuria decreased by 32% vs. UC rats. Enalapril alone, or in combination with paricalcitol, further decreased proteinuria (~70%). Glomerulosclerosis and interstitial infiltration increased in UC rats. Paricalcitol and enalapril inhibited this. The increase in cardiac atrial natriuretic peptide (ANP) seen in UC rats was significantly decreased by paricalcitol. Enalapril produced a more dramatic reduction in ANP. Renal oxidative stress plays a critical role in inflammation and progression of sclerosis. The marked increase in p22(phox), a subunit of NADPH oxidase, and decrease in endothelial nitric oxide synthase were inhibited in all treated groups. Cotreatment with both compounds inhibited the uremia-induced increase in proinflammatory inducible nitric oxide synthase (iNOS) and glutathione peroxidase activity better than either compound alone. Glutathione reductase was also increased in UE and UP rats vs. UC. Kidney 4-hydroxynonenal was significantly increased in the UC group compared with the normal group. Combined treatment with both compounds significantly blunted this increase, P < 0.05, while either compound alone had no effect. Additionally, the expression of Mn-SOD was increased and CuZn-SOD decreased by uremia. This was ameliorated in all treatment groups. Cotreatment with enalapril and paricalcitol had an additive effect in increasing CuZn-SOD expression. In conclusion, like enalapril, paricalcitol alone can improve proteinuria, glomerulosclerosis, and interstitial infiltration and reduce renal oxidative stress. The effects of paricalcitol may be amplified when an ACE inhibitor is added since cotreatment with both compounds seems to have an additive effect on
ameliorating uremia-induced changes in iNOS and CuZn-SOD expression, peroxidase activity, and renal histomorphometry.

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