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Kidney and aging

L. Ferder
Universidad de Buenos Aires. Argentina.

The progressive development of glomerulosclerosis is a well-known phenomenon that occurs in the aging kidney and in a variety of experimental models of renal injury. In the remnant kidney model, Brenner y cols.,[1] had demonstrated that ACE inhibitos and angiotensin II antagonists can attenuate glomerulosclerosis. They also showed that both types of compound can lower intraglomerular pressure by altering the resistance of the efferent arteriole. Based on these findings they proposed that glomerular hyperfiltration is an underlying factor in the development of glomerulosclerosis.

In a previous report we demonstrated that enalapril, administered to mice during 24 months, significantly decreased mesangial expansion, glomerulosclerosis and the loss of glomeruli normally associated to aging[2]. In other models, the decrease of intraglomerular pressure by ACE inhibitors, as well as angiotensin II antagonists, accounts for the attenuation of glomerular injury[3].

In addition to its protective actions on glomerular structure, chronic enalapril administration has been shown to decrease both peritubular and medullar interstitial sclerosis in aging mice[4,5].

In an attempt to further define the role of the renin-angiotensin system in aging, we administered enalapril (10 mg/kg/day) and the angiotensin II receptor antagonist losartan (30 mg/kg/day) to Wistar rats since weaning.

After 7 months of treatment, both of losartan and enalapril significantly decreased tubular atrophy and glomerular and interstitial fibrosis (table I).

The protective effect of losartan and enalapril in the kidneys of the animals at 18 and 22 months was also analyzed. Reduced kidney damage was absolutely clear, losartan group presented lower glomerular and tubulointerstitial fibrosis, monocytic/macrophage infiltrates and tubular atrophy than control animals (F. Inserra, I. Stella, M. L. Kurnek, N. Terragno, N. Paglia, N. Basso, L. Ferder: losartan and enalapril protect gainst age related kidney lesions in normal rats treatd for 18 months of age [abstract]. 16th Scientific Meeting of the American Society of Hypertension, may 2001, San Francisco, USA). The difference found by electron microscopy in the cells of the proximal tubule at 18 months between control and losartan groups is outstanding, mainly related to higher brush border size and amount of mi-

Table I. Kidney fibrosis. Effects of losartan and enalapril

	Control	Enalapril	Losartán
Interstitial fibrosis (%)	1.39 ± 0.13	0.26 ± 0,8*	0.39 ± 0.07*
Tubular atrophy (%)	1.22 ± 0.12	0.05 ± 0.05*	0.16 ± 0.08*
Collagen-III (%)	1.17 ± 0.12	0.44 ± 0.10*	0.80 ± 0.12*
α-SM-actin (%)	0.89 ± 0.14	0.11 ± 0.07*	0.39 ± 0.14*

These results were evaluated by a semiquantitative score 0-4.
*p < 0.05 *vs* control. ANOVA Test.

Table II. Losartan and enalapril protect against age related kidney lesions in normal rats treated from 12 to 18 months of age

	PGF	MM	FS	TD	ICF	IMF	α-A
Control	2.71 ± 1.11	2.71 ± 0.95	1.64 ± 0.85	2.36 ± 0.63	2.79 ± 0.39	1.93 ± 0.89	1.29 ± 1.07
Losartan	2.00 ± 0.29	1.00 ± 0.41	0.83 ± 0.37	1.50 ± 0.82	2.08 ± 0.45	1.17 ± 0.24	1.08 ± 0.67
Enalapril	0.83 ± 0.55	0.58 ± 0.34	0.08 ± 0.19	0.60 ± 0.34	1.00 ± 0.50	0.10 ± 0.18	0.40 ± 0.34

A score evaluation was applied; lesions were considered as 0 = normal; 1 = slight; 2 = moderate and 3 = severe.
*p < 0.05 vs C. PGF; periglomerular fibrosis; MM: mesangial matrix; FS: focal sclerosis; TD: tubular dilation; ICF: interstitial cortical fibrosis; IMF: interstitial medullar fibrosis; α-A: α-SM-Actin. In summary, losartan and enalapril treatment from 12 to 18 months of age preserve renal function and structure from changes due to aging in the normal rat.

tochondria in losartan treated animals as well as conservation of mitochondrial ultra structure and function, similar to younger animals.

Finally, we were interested to find out if this protective effect should be produced if the treatment would have been started in older animals. Because of that, we repeat the experiments but in this opportunity the treatment was started at 12 months of age of the animals and the results were evaluated at 18 months. The results can be seen in table II (F. Inserra, I. Stella, M. L. Kurnek, N. Terragno, N. Paglia, N. Basso, L. Ferder: losartan and enalapril protect against age related kidney lesions in normal rats treated from 12 to 18 months of age [abstract]. *J Am Soc Nephrol* 12; 679A, 2001).

These data suggest that the renin-angiotensin system plays a role in the natural aging of the kidney.

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