No Additive Effect of the Combined Therapy with Cilazapril and Losartan on the Progression of Adriamycin-Induced Nephropathy

HJ Kim, SW Han, JH Ryu, IG Park*, SS Paik†
MH Park†, HS Chung†, SW Kim§, JU Lee§

Depts of Nephrology, Clinical Pathology, Pathology† and Anatomy†, Hanyang University Medical School, Seoul, Chonnam National University Research Institute of Medical Sciences§, Gwangju, Korea*

Background : The effects of angiotensin-converting enzyme inhibitor(ACEi) and angiotensin receptor blockade(ARB), either alone or in combination, on the progression of adriamycin-induced glomerulopathy were examined.

Methods : Male Sprague-Dawley rats(180-250 g), 6 weeks after adriamycin(ADR) 2 mg/kg iv once and without it as control, were divided into 5 groups : control without ADR(CTR, n=5), ADR only(ADR, n=6), ADR+cilazapril 1 mg/kg/d orally(ACEi, n=7), ADR+losartan 5 mg/kg/d orally (ARB, n=7), and cilazapril 1 mg/kg/d+losartan 5 mg/kg/d both(ACEi+ARB, n=7). At the end of the 12th week, TGF $beta_1$ and laminin $beta_1$ mRNA expression of renal cortex by RT-PCR, and histopathologic scoring of glomerulosclerosis(GS) were performed on sacrificing.

Results :

	CTR	ADR	ACEi	ARB	ACEi+ARB
BP-12 wk	120±2.9	126±1.5	110±2.2*, ‡	112±2.8*, §	107±3.3*, §
Ccr-12 wk	19±2.2	13±1.4	18±2.2	19±2.1	19±3.5
Urine P/Cr	4.8±1.0	47.0±8.3	12.4±4.5*, §	19.4±6.7*, §	18.5±4.6*, §
GS	1.4±0.4	10.7±2.7	0.8±0.4*, §	2.6±1.0*, §	1.7±1.5*, §
TGF $beta_1$	1.0±00	1.6±0.03†	1.2±0.04§	1.3±0.03§	1.2±0.04§
Laminin $beta_1$	1.0±00	1.5±0.05†	1.4±0.06†	1.5±0.08†	1.4±0.07†

All data are mean±SEM, Urine P/Cr; 24-hr urine protein to creatinine ratio
**p<0.01 vs ADR, †p<0.05 vs CTR, ‡p<0.01 vs CTR, §not significant vs CTR*

Marked anti-proteinuric effect was accompanied with limiting progressive glomerulosclerosis and decreased TGF $beta_1$ expression similarly in either ACEi or ARB, but no further changes in combination of both. However, enhanced expression of laminin $beta_1$ by ADR was not attenuated significantly on RAS blockade.

Conclusion : Our data showed no additive effects of ACEi and ARB on the progression of adriamycin-induced glomerulopathy. It is also suggested that expansion of extracellular matrices as a hallmark of progressive glomerulosclerosis is in part independent of RAS.