

**Losartan attenuates apoptosis and fibrosis in adriamycin-induced cardiomyopathy rat model.**

*Hong Y.M., Kim K.C.*

*Departments of Pediatrics (1); Thoracic and Cardiovascular Surgery(2), Ewha Womans University School of Medicine, Seoul, Korea*

**Purpose:** The precise mechanism for the pathogenesis in adriamycin (ADR)-induced cardiomyopathy has not been elucidated. Different hypotheses include the production of free radical species, an interaction with nucleic acid or nuclear components and disruption of a cardiac-specific program of gene expression. Programmed cell death or apoptosis has been proposed to be involved in cardiac dysfunction under some experimental and clinical conditions. Angiotensin (AT) II plays an important role in cardiac fibrogenesis by acting as a potent growth factor and cytokine for vascular smooth muscle cells, cardiac myocytes and cardiac fibroblasts, via activation of the AT type I receptor. Losartan is a selective AT1 receptor antagonist. It improves left ventricle function, prevents geometric remodelling, and prolongs survival in several heart diseases, such as hypertension, heart failure, ischemic heart disease, and diabetes mellitus. The purpose of this study was to investigate the changes of apoptosis and remodelling in adriamycin induced cardiomyopathy rat model after losartan treatment.

**Methods:** Male Sprague–Dawley rats were separated into three groups: the control group (C group), A group (ADR 5 mg/week for 3 weeks, intraperitoneal injection), L (losartan group) was treated with ADR (5 mg/week for 3weeks) and losartan (10 mg/kg/day for 3 weeks). The rats were sacrificed at week 3. Changes of caspase-3, B cell leukemia/lymphoma (Bcl)-2, Bax, tumor necrosis factor (TNF)- $\alpha$ , matrix metalloproteinase (MMP)-3, collagen 1 and collagen 3 proteins were estimated by westernblot analysis in the heart tissues after losartan treatment. Left ventricle was stained by Masson's Trichrome for evaluation of collagen contents.

**Results:** Left ventricular hypertrophy was significantly noted in the A group and it was significantly decreased in L group compared with A group. The protein expressions of caspase-3, Bax, MMP-3, TNF- $\alpha$ , collagen 1 were significantly higher in the A group compared with the C group. They were significantly decreased after losartan treatment.

Protein expression of Bcl-2 was decreased in L group, but it was not significantly different. Collagen contents in LV were significantly increased in A group compared with C group and decreased in L group compared with A group.

**Conclusion:** Losartan decreased apoptosis, inflammation and fibrosis in LV tissues.