25) Effects of Lisinopril on Regression of Left Ventricular Hypertrophy, Cardiorenal Hemodynamics and Neurohumoral Factors in SHR.

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The presence of left ventricular hypertrophy (LVH) appears to increase the incidence of arrhythmias and sudden death. Regression of LVH is, therefore, one of the important goals for hypertension treatment. However, cardiac and renal hemodynamics of the regressed heart is still controversial. The purpose of this study was to evaluate cardiorenal hemodynamics of the regressed heart with lisinopril in mature SHR, using cardiac catheterization.

Lisinopril (5mg/kg/day) was orally administered to ten 15-week-old male SHR for 20 weeks; 10 age- and sex-matched SHR given placebo served as control. Conscious blood pressure (tail-cuff method) and body weight (BW) were measured every 2 weeks. Under pentobarbital anesthesia (45mg/kg, i.p.), a catheter (PE 50) was inserted to the right atrium (RA) via the right jugular vein to be used for injections. A 2F Mikro-Tip® catheter (SPC-320, Millar Inc. U.S.A.) was introduced through the right carotid artery into the ascending aorta to record aortic pressure; the catheter was advanced to the left ventricle (LV) for measurements of LV pressure, its first derivative (dp/dt), and LV end-diastolic pressure (LVEDP). LV pressure decay during LV isovolumic relaxation period, or time constant T, was obtained according to the method of Weiss et al. (J Clin Invest 58: 751, 1976). Cardiac output was determined by the thermodilution method (Cardiotherm 500, Columbus Inc. U.S.A.). Renal blood flow (RBF) and hindquarter muscle flow were measured by laser doppler flowmetry (ALF2100, Advance Inc. Japan). Mean arterial pressure (MAP), cardiac index (CI), stroke volume index (SI), and total peripheral resistance index (TPRI) were calculated. To assess LV response to acute rise in LV pre- and afterload, physiological saline and angiotensin II (ANG II) were injected, respectively, through the RA catheter. Blood samples for plasma renin activity (PRA), ANG II, norepinephrine (NE), epinephrine (E), and atrial natriuretic hormone (ANP) were drawn from the carotid artery of another age- and sex-matched treated and untreated SHR, in which no hemodynamic study was performed. At the completion of the hemodynamic measurements, the heart was arrested with an intravenous injection of 2% procaine and right and left ventricular and kidney weights were determined. The experiment was performed 48 hours after the latest dose of lisinopril.

Conscious systolic blood pressure was significantly decreased in the treated SHR compared to that of the untreated SHR (P<0.001). BW and LV/BW were smaller in the treated rats than in the untreated rats (P<0.01, P<0.001, respectively). In the treated rats, MAP and TPRI were significantly decreased (P<0.001) and hindquarter muscle flow tended to be increased than in the untreated rats. No significant differences were present in heart rate, LVEDP, CI, SI, time constant T, and RBF/BW. During afterload elevation with ANG II, LV systolic pressure rose about 30 mmHg; RBF/BW similarly decreased (P<0.01) in the two groups of rats but the other hemodynamic parameters did not change. During preload elevation with saline, CI, SI, and RBF/BW increased (P<0.01 for each) without difference between the two groups. While plasma catecholamine (NE and E) levels were unchanged, PRA was higher (P<0.01) and ANP was lower (P<0.05) in the treated rats than in their counterparts.

Chronic treatment with lisinopril significantly decreased blood pressure in mature SHR, without compromising RBF, and it also decreased BW and ANP, suggesting that lisinopril possesses a diuretic property due to renal vasodilation. LV function of the regressed heart with lisinopril was well maintained at rest and during acute LV pre- and afterload elevation. Besides afterload reduction, the inhibition of the renin-angiotensin system may play an important role in the regression of LVH by lisinopril.