7) Relationship between the regression of cardiac hypertrophy and myosin isoenzyme pattern in SHR

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It is interesting whether cardiac hypertrophy caused by hypertension is regressive or not with medicinal treatment. Four anti-hypertensive drugs (α -Methyldopa, Captopril, Hydralazine, Nicardipine) were administered to SHR in order to examine the regression of cardiac hypertrophy. We also report the effects of anti-hypertensive drugs on cardiac contractile proteins in SHR.

Methods; 23-week-old male SHR were divided into 4 groups. Each group was treated with α -methyldopa(150mg/day), captopril(20mg/day), hydralazine(30mg/day) and nicardipine(30mg/day) respectively. Four drugs were administered orally mixed with powdered food for 8 weeks. Blood pressure and heart rate were measured once a week. Heart to body weight ratio, left ventricular myosin Ca^{2+} -ATPase activity, myosin isoenzyme pattern, DNA and collagen content were measured. Myosin was prepared according to Weber-Edsall et al. Myosin Ca^{2+} -ATPase activity was determined by measuring inorganic Pi liberated when ATP was added. Myosin isoenzyme was separated by the Na-pyrophosphate gel (T=4%, C=3% PAG) electrophoresis described by Hoh et al. The electrophoresis was carried out for 30 hours at a voltage gradient of 13V/cm. DNA was measured as described by Schneider et al. And we measured hydroxyproline concentration as represents collagen content.

Results; Blood pressure of treated groups decreased, whereas that of non-treated group remained 220±12mmHg. The blood pressure of captopril- or hydralazine- treated group was lower than that of α -methyldopa- or nicardipine-treated group. The blood pressure of the former two groups reduced to 130-140mmHg and that of the latter two groups only to 180-195mmHg. The heart to body weight ratio of the captopril-treated group showed a decrease of 26% as compared with non-treated group. Although the blood pressure reduced in the same degree with captopril-treated group the heart to body weight ratio of the hydralazine-treated group decreased only 5%. Still more, the ratio of hydralazine-treated group was higher than that of α -methyldopa-treated group whose blood pressure reduced mildly. In captopril- and hydralazine-treated group, blood pressure reduced remarkably, the left ventricular myosin Ca^{2+} -ATPase activity showed an increase by 20-30% as compared with non-treated group. Moreover, myosin V_1 fraction was increased, and V_3 fraction was decreased in these groups as compared with non-treated group. However, in α -methyldopa and nicardipine group, blood pressure reduced mildly and distinct alterations in isoenzyme pattern were not obtained. Besides, the increase of myosin V_1 in captopril-treated group was more remarkable than that in hydralazine-treated group, inspite of similar reduction of blood pressure in both groups. DNA content decreased only in captopril-treated group as compared with non-treated group. There was no difference in hydroxyproline content between the treated groups and non-treated group.

Conclusion; In our present study the decrease of blood pressure by anti-hypertensive drugs did not always reduce the regression of cardiac hypertrophy and (did not always) alter left ventricular myosin isoenzyme pattern. From these results it can be said that, in SHR, pressure-overload is not only the factor which effects on (the regression of) cardiac hypertrophy or the alteration of left ventricular myosin isoenzyme pattern. Other mechanisms (changes of sympathetic nervous system, for example) may also be involved; but further enamination will be necessary. So it is important to select anti-hypertensive drugs, if we hope the regression with unchanged collagen and normalized cardiac contractile proteins.