11) Differential Effects of Various Antihypertensive Agents on Cardiac Hypertrophy in Stroke-prone SHR (SHRSP). Yukio Yamori*^{o+}, Robert C. Tarazi* and Akira Ooshima*^{o+}. International Center*, Cleveland Clinic, Cleveland, Ohio, U.S.A., Japan Stroke Prevention Center⁺ and Department of Pathology^o, Shimane Medical University, Izumo 693.

INTRODUCTION

Recent observation from our laboratories have demonstrated that SHR, especially SHRSP develop cardiac hypertrophy --- meaning a significant increase in heart weight in comparison with age-matched Wistar-Kyoto rats (WKY) --- even during prehypertensive or early hypertensive stages. Furthermore, the degree of cardiac hypertrophy (CH) seems to parallel the medial hypertrophy of arterial walls, suggesting that CH might be a good indicator of vascular hypertrophy or hyperplasia. Yamori et al (EUROP J PHARMACOL 38: 349, 1976) first indicated that effects of various antihypertensive agents on vascular protein synthesis differed, despite their equipotent blood pressure control; the difference in vascular protein synthesis was apparently related to the degree of sympathetic stimulation or suppression achieved by the drug. Sen et al. (CARDIOVASC RES 11: 427, 1977) noted a similar discrepancy between antihypertensive effect of some agents and their effect on CH. The common observation in both studies is that vasodilators such as hydralazine lower blood pressure but do not effectively reduce cardiac weight in SHR in contrast with sympathetic inhibitors which effectively reduce both arterial pressure and ventricular weight. In this study, we have further extended these studies both to other antihypertensive agents (converting enzyme inhibitor) and to different routes of administration (intracisternal infusion). Moreover, we have attempted to determine if short periods of therapy can prevent cardiac structural changes.

MATERIALS AND METHODS

Young SHRSP at the age of 7 weeks, 30 in total, were divided 5 in each into the following 6 groups: non-treated group, α -methyl dopa (A) (250 mg/kg, p.o.), hydralazine (H) (8 mg/kg, p.o.), β -blocker (B) (propranolol, 50 mg/kg, p.o.), converting enzyme inhibitor (CEI) (SQ 14,225, 70 mg/kg, p.o.) and central α -methyl dopa treatment (CA) (continuous intracisternal infusion 20 μ g/ μ l·h with an Alzet osmotic minipump). Five age-matched Wistar-Kyoto rats (WKY) were also used as a non-treated control group. After 2 weeks of therapy during which repeated measurements of indirect blood pressure levels were obtained, rats were sacrificed and heart weights (left and right ventricles) were determined.

RESULTS

(1) Effective treatments which blocked the quick development of hypertension in SHRSP were A, CA, H and CEI, while B had no effect on the development of severe hypertension.

(2) A, CA and CEI, significantly reduced heart weights concomitant with blood pressure control; in contrast, H did not decrease heart weight in spite of blood pressure reduction. In B-treated group the absolute heart weight was significantly less than the nontreated group, but no difference was observed in heart to body weight ratio because of the reduced gain in body weight.

CONCLUSION WITH DISCUSSION

There was a clear discrepancy among various antihypertensive agents between their effect on blood pressure and that on heart weight. These results confirm our previous observations but also demonstrate that structural changes could be observed as early as after two weeks of treatment. In view of Yamori's results correlating cardiac and vascular alteration in SHRSP, study of heart weight could be an effector rapid enough to analyze various forms of treatment. Further, results with CA seem to indicate that the action of MD is probably mediated through its central autonomic action rather than a local effect of the drug. Finally, CEI was shown to be effective in reversing cardiac hypertrophy; this could be related in part to recent findings showing that its antihypertensive effect was not associated with reflex sympathetic stimulation. Young SHRSP which quickly develop hypertension and CH may be regarded as a good model for the evaluation of the effect of antihypertensive agents on cardiac and vascular structural changes.