2) Effects of Captopril on Mean Blood Pressure, Plasma Renin Concentration and Bradykinin in SHR and SHR-SP. Osamu Kida, Yasuyuki Morotomi, Noriyuki Someya, Kenji Kodama, Toshinobu Higa, Koichi Kondo and Kenjiro Tanaka. First Department of Internal Medicine, Miyazaki Medical College, Kiyotake, Miyazaki 889-16. Tomoyoshi Nishino. Otsuka Assay Laboratories, Otsuka Pharmaceutical Co., Ltd., Tokushima 771-01.

Angiotensin I converting enzyme inhibitor, captopril, is considered to suppress the renin-angiotensin system and to activate the kallikrein-kinin system simultaneously by blocking degradation of bradykinin. In present work, effects of captopril on mean blood pressure (MBP), plasma renin concentration (PRC) and plasma bradykinin (BK) were studied in spontaneously hypertensive rats (SHR) and stroke prone SHR (SHR-SP) and Wistar-Kyoto normotensive rats (WKY) to clarify the mode of action of captopril.

Twenty to 23 weeks aged WKY, SHR and SHR-SP were anesthetized with intra-peritoneal injection of pentobarbital (35 mg/Kg), and catheterized in left carotid artery for direct measurement of MBP. Captopril (100 mg/Kg, solved in 5% glucose) was administrated orally in six rats of each strains (captopril group), and vehicle (5% glucose) was administrated in another six rats (control group). PRC and BK were measured after recording of MBP for 60 minutes. In order to estimate the effect of aging on the responsiveness of captopril, twelve SHRs were added to captopril group: seven rats were 10 weeks age and five were 30 weeks age.

Mean age and mean body weight were not significantly different in both groups in all strains. Basal MBPs were 120.3 ± 3.7 mmHg in control group and 121.5 ± 3.4 mmHg in captopril group in WKY, 183.4 ± 5.5 mmHg and 189.6 ± 9.0 mmHg in SHR, and 211.2 ± 7.4 mmHg and 213.3 ± 13.3 mmHg in SHR-SP respectively. Basal MBPs were not significantly different in both groups for all strains.

	WKY		SHR		SHR-SP	
	control	captopril	control	captopril	control	captopril
reduction in MBP (%)	0.6 ± 0.6	2.7 ± 2.4	0.4 ± 0.6	$7.5 \pm 1.0^{**}$	0.8 ± 1.9	$13.9 \pm 2.9^{**}$
PRC (ng/ml/hr)	58.0 ± 5.1	$1796.8 \pm 190.0^{**}$	54.8 ± 10.3	$335.0 \pm 99.9^*$	163.8 ± 7.7	$472.7 \pm 117.2^*$
BK (pg/ml)	21.7 ± 2.9	29.7 ± 3.7	27.4 ± 6.5	32.8 ± 2.6	16.9 ± 2.2	$33.4 \pm 6.3^*$

mean $\pm$ SE, *: $p < 0.05$, **: $p < 0.01$; control vs captopril. n = 6 in each group.

Table showed the percent reduction in MBP, PRC and BK 60 minutes after administration of captopril or vehicle. Reduction in MBP was significantly greater in captopril group than in control group in SHR and SHR-SP, but the same result was not seen in WKY. PRC was significantly high in captopril group in all strains, especially so in WKY. And BK was significantly high in captopril group only in SHR-SP.

There was a significant correlation between age and PRC on captopril treated SHR ($r = -0.59$, $p < 0.01$). But the same correlation was not seen between age and reduction in MBP or between age and BK.

MBP was reduced by captopril in both SHR and SHR-SP. But it was greater in the latter because the former was a normal renin type and the latter was a high renin type. Especially in SHR-SP, it was demonstrated that captopril produced the increase in BK associated with the reduction in MBP. These results suggested that BK might participate, in part, the reduction in blood pressure by captopril.

PRC was significantly increased by captopril in WKY, SHR and SHR-SP. These observations indirectly suggested that captopril inhibited the conversion of angiotensin I. PRC was markedly increased in normotensive WKY and young SHR in particular. It was also suggested that the increase in PRC by captopril was blunted in proportion to development or maintenance of hypertension.