- 39) Relationships between the anti-hypertensive and vascular healing effects of SQ 29,852, manidipine, captopril and hydralazine on M-SHRSP. Taka-aki Chikugo, Yoshio Ohta and Koza Okamoto. Department of Pathology, Kinki University School of Medicine, Osaka, 589.

Introduction:

We histopathologically studied the effects of several anti-hypertensive drugs on the brains, kidneys and certain other organs of M-SHRSP. It has been shown that in rats such symptoms as disturbance of movement and paralysis of extremities, as well as vascular changes in the brain and other organs observed before administration of angiotensin converting enzyme inhibitors or calcium antagonists disappear within a short time. Under optimum doses of angiotensin converting enzyme inhibitors, these changes have come about in spite of continued high blood pressure. In this experiment, we examined the relationships among different dosages of certain anti-hypertensive drugs, their anti-hypertensive effects and vascular changes found in the several organs.

Materials and methods:

223 11-week-old male M-SHRSP were used. Angiotensin converting enzyme inhibitors (captopril or SQ 29,852) (Bristol-Myers Squibb, K.K. Japan), a calcium antagonist (manidipine hydrochloride) (Takeda Chemical Industries, Ltd., Osaka), or a vascular smooth muscle relaxant (hydralazine hydrochloride) (CIBA-GEIGY Co., Ltd. Japan) were administered separately to 4 groups of rats. SQ 29,852 or manidipine was administered orally in doses of 2, 5, 10, 20, 40, 60 or 80 mg/kg/day (mixed in Funabashi SP) to 7 separate subgroups. Some of the rats were given a combination of SQ 29,852 (20mg/kg/day) and manidipine (20mg/kg/day). Captopril, 40 mg/kg/day, (mixed in Funabashi SP) was administered orally and hydralazine, dosage approx. 15 mg/kg/day, (80 mg/l, in drinking water) was given at will. Body weights and blood pressures (using the tail-pulse pickup method) were measured before, periodically during, and after treatment. All rats were sacrificed as appropriate and autopsied in order to histopathologically examine the organs.

Results:

Body weights gradually increased in all groups. Rats given 2, 5, 10, 20 mg/kg/day SQ 29,852 separately showed only a weak anti-hypertensive effect with blood pressures remaining over 250 mmHg. Angioneclerosis were still recognized following administration of SQ 29,852 at 2 or 5 mg/kg/day. However, with treatment at either 10 or 20 mg/kg/day the angioneclerosis disappeared within 20 days. Rats given SQ 29,852 at 40, 60 or 80 mg/kg/day evidenced a strong anti-hypertensive effect and their angioneclerosis disappeared within 10, 10 or 4 days, respectively. On the other hand, the separately treated manidipine subgroups, given doses of 2, 5 or 10 mg/kg/day showed only a weak anti-hypertensive effect with high blood pressures remaining at over 250 mmHg and with angioneclerosis continuing to be recognized in all instances. For rats given manidipine at a rate of 20 mg/kg/day, blood pressures dropped to around 210 mmHg and angioneclerosis disappeared within 8 days. With manidipine treatment at 40 or 80 mg/kg/day, blood pressures lowered remarkably and angioneclerosis disappeared within 10 or 5 days, respectively. For combined SQ 29,852 and manidipine treatment at 20 mg/kg/day, blood pressures lowered to around 210 mmHg and the disappearance of angioneclerosis was recognized within 8 days. Blood pressures for the captopril and the hydralazine treatment groups remained around 250 mmHg, but angioneclerosis disappeared in the former group within 18 days, about twice the time it took when using similar doses of SQ 29,852 or manidipine. For the hydralazine treated group angioneclerosis did not disappear in any of the organs.

Summary:

Anti-hypertensive drugs (SQ 29,852, manidipine, captopril or hydralazine) were administered to 11-week-old male M-SHRSP. For rats given the first 3 of these drugs, angioneclerosis of the brain, kidneys and certain other organs disappeared, but angioneclerosis did not disappear in the hydralazine-treated rats. Among the groups given the three effective drugs, rats given SQ 29,852 also showed that the degree of the anti-hypertensive effect does not consistently correlate with the disappearance of angioneclerosis.