Relationship between Blood Pressure and Humoral Factors in Inhibition of Hypertension with Long-Term Administration of Antihypertensive Agents in SHRs from Prehypertensive Stage

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In order to elucidate the hypertensive mechanisms of the SHR, various anti-hypertensive drugs were administered to SHRs of pre-hypertensive stage, their blood pressure responses and changes of humoral factors were observed.

Materials and Methods:

Fusaric acid 150 mg/Kg/day, hydralazine 30 mg/Kg/day, propranolol 30 mg/Kg/day, which were mixed with normal stock diet containing 0.24% sodium were administered to SHRs from 5 weeks of age. Plasma catecholamines (PCA) and plasma renin activities (PPA) were measured before treatment and 5 weeks and 10 weeks after the beginning of the administration of the above-mentioned diet. The data were compared with those of non-treated age-matched SHR controls. Each group consisted of more than 8 SHRs and blood samples were taken immediately after decapitation. PCA was measured by double isotope derivative method and PRA by bioassay method. Occasional blood pressure (BP) measurements were done by the tail-pulse-pickup method.

Results:

Body weight increased similarly in each group as well as in the control group. Before treatment, the mean of the BP was 110 mmHg. At 10 weeks of age, 5 weeks after starting the experiment, the mean of the BP of the control group increased to 151 mmHg and those of fusaric acid-, hydralazine-, and propranolol-treated groups were 116 mmHg, 132 mmHg, and 135 mmHg, respectively. At 15 weeks, the mean of the BP of the control group increased to 161 mmHg and fusaric acid, hydralazine, propranolol groups were 120, 132, and 160 mmHg. The inhibition of hypertension was seen in fusaric acid and hydralazine groups, but in propranolol group BP increased in the same way as in the control group. PCA of the control group at 5 weeks, 10 weeks, and 15 weeks of age were 0.43 µg/L, 0.76 µg/L, and 0.81 µg/L, the latter 2 of which were significantly higher than the first one. The PRA of control group was 18.2 ng/ml/18 hrs at 5 weeks, 29.7 ng/ml/18 hrs at 10 weeks and 35.9 ng/ml/18 hrs at 15 weeks. In fusaric acid group, PCA was 0.49 µg/L at 10 weeks of age and 0.62 µg/L in 15 weeks, which remained significantly lower level.

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than control group at both age. Although hypertension was inhibited, PRA of this group was 37.5 ng/ml/18 hrs at 10 weeks and 43.3 ng/ml/18 hrs at 15 weeks, which was significantly higher than that of the control group. In hydralazine group, PCA was 0.75 µg/L at 10 weeks and 0.71 µg/L at 15 weeks; this response was similar to that of control group. PRA of this group was 37.6 ng/ml/18 hrs at 10 weeks and 44.6 ng/ml/18 hrs at 15 weeks, which was significantly higher than that of control group. In propranolol group, PCA was 0.58 µg/L at 10 weeks and 0.65 µg/L at 15 weeks. In this group, hypertension developed but PCA was lower than in the control. The PRA in this group was 27.0 ng/ml/18 hrs at 10 weeks and 34.8 ng/ml/18 hrs at 15 weeks; this response was not different from the control.

**Discussion:**

We have reported that the pathogenesis of the hypertension of SHR was not entirely but largely related to catecholamine level. In this experiment, fusaric acid-administered SHR group showed a remarkable inhibition of both hypertension and PCA level, which seems to support our opinion. However, in hydralazine group, in spite of high PCA level, hypertension did not develop. And so, it should be considered that factors other than catecholamines would be related to the maintenance of high blood pressure. In this experiment, no definite relation could be recognized between PRA level and hypertension.