Effects of Antihypertensive Drugs on the Hemodynamics of SHR

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We have previously reported the hemodynamic differences between spontaneously hypertensive rat (SHR) and normotensive Wistar rat (WR). Blood pressure and systemic vascular resistance were higher in SHR than WR, and heart rate was increased in SHR. Administration of propranolol decreased cardiac output, but increased blood pressure and systemic vascular resistance in SHR.

We concluded that there was elevation of sympathetic tone with increased responsiveness to α- and β-adrenergic blockers in SHR. We also reported the hemodynamic changes induced by the selective β-blockers, practolol and H35/25, in SHR, in the last meeting of the Spontaneously Hypertensive Rat. We showed that hemodynamic changes caused by β-blockers in SHR could be explained as both species specific and dose dependant. However, the above results obtained in SHR's seemed to be too premature to extrapolate to humans or dogs (Sasaki et al: Jap Heart J 18: 515, 1977). Our experiment was designed to study the differences of the hemodynamic between the prehypertensive and established-hypertensive stages of SHR, and to elucidate which hypotensive drug was the most effective in the treatment of hypertension of SHRs.

Materials and Methods:

SHR of 4 weeks (SHR[4W]) and 14 weeks (SHR[14W]) of age were used in this experiment. Animals were anesthetized by light ether, α-chloralose and gallamine. The trachea was cannulated and ventilation was maintained by artificial respiration. The chest was opened by median sternotomy, and an electromagnetic flow probe was placed around the thoracic aorta for measurement of cardiac output (COP). Blood pressure (BP) was measured by a catheter inserted in either the femoral artery or carotid artery. Drugs were administered via a catheter inserted into the jugular vein. Hydralazine, phentolamine, and hexamethonium were used. The doses ranged from 0.01 μg/100 Gm to 100 μg/100 Gm, at a volume of 0.05 ml/100 Gm. Systemic vascular resistance (SVR) was calculated from the mean BP and the COP, and was expressed by mmHg/ml/min/100 Gm. Each parameter was measured at its peak after drug infusion. Student’s t-test was used for the statistical analysis.
Results:
(1) SBP, DBP, and TPR were significantly higher in SHR [14W] than in SHR [4W].
(2) COP was significantly higher in SHR [4W] than in SHR [14W].
(3) BP was decreased by hydralazine in both groups, and the reduction was significantly larger in SHR [14W] than in SHR [4W]. COP tended to increase.
(4) BP decreased significantly with phentolamine in both groups, and it was more marked in SHR [14W] than in SHR [4W]. COP was increased by phentolamine, and decreased by hexamethonium.

Conclusion:
There is an elevation of sympathetic tone (Furukata et al: Jap Heart J 18: 513, 1977), which may be due to abnormalities of catecholamine synthesis in the central nerves system, in SHR (Hashida: Folia Endocrinol Jap 49: 80, 1973).

We have previously reported that blood pressure and systemic vascular resistance were higher in SHR than in WR (Sasaki, Kubota et al: Jap Heart J 17: 361, 1976). The evidence that the blood pressure was lower and the COP was larger in SHR [4W] than in SHR [14W] suggests the causative effect of the increased systemic vascular resistance in the hypertension of SHR.

The elevation of blood pressure and systemic vascular resistance may be followed by the decrease of cardiac output. The results demonstrate that catecholamine antagonists may be the most effective in the prevention of hypertension in SHR.