The Role of Histamine and Catecholamine on the Blood Pressure Regulation Mechanism in Spontaneously Hypertensive Rats

Itaru YOMAIDA,* Yoshio MONMA,*** and Hideya SAITO**

It has been reported that vasoactive amines such as catecholamine are related to the blood pressure regulation mechanism. It has been already realized that histamine has a physiological action opposite to norepinephrine in blood pressure regulation. But no precise conclusion have been obtained regarding the role of histamine in blood pressure regulation. The present experiments were undertaken to examine histamine and catecholamine content in various tissues in spontaneously hypertensive rats (SHR). The effect of clonidine on these biogenic amines in SHR was also studied.

Methods :

In the experiments we used male SHR (Okamoto-Aoki) and Wistar Kyoto rats (WKY) donated by department of pharmacology, Jichi Medical school (Tochigi, Japan). Endogenous histamine was measured by enzymatic double isotopic method. Endogenous catecholamine was assayed by the method of THI reaction. For the measurement of blood pressure and heart rate, the tail plethysmographic method was used. In the experiments for the turnover rate of ^3H -norepinephrine in brainstem, the method by Glowinski and Axelrod was used. ^3H -norepinephrine at a dose of 5 $\mu\text{Ci}/\text{rat}$ was injected into the lateral ventricle, and at 1, 12, and 24 hours after the injection, the rats were decapitated and the ^3H -norepinephrine of the brainstem was measured. In the experiments of the turnover rate of ^3H -norepinephrine in heart, ^3H -norepinephrine at a dose of 20 $\mu\text{Ci}/\text{Kg}$ was injected into femoral vein. For the measurement of ^2H -norepinephrine, Packard's sample oxidizer and liquid scintillation counter were used. From the disappearance curve of the ^3H -norepinephrine the turnover rate of norepinephrine was obtained by norepinephrine content ($\mu\text{g}/\text{Gm}$) $\times$ elimination rate constant (hr^{-1}). In the experiments for the effect of clonidine on histamine and catecholamine content in SHR, 1 month administration of clonidine (300 $\mu\text{g}/\text{Kg}/\text{day}$ p.o.) was studied. SHR [14 weeks of age, systolic blood pressure $212.7 \text{ mmHg} \pm 3.0$ (S.E.), heart rate $425 \text{ beats}/\text{min} \pm 9.0$ (S.E.)] was divided into 2 groups. The first group of SHR was as the control group and fed on oriental rat chow as the regular diet. The second group of SHR was taken as clonidine administered group and fed on clonidine mixed diet. In the test diet, clonidine was thoroughly mixed with regular diet at a rate of $4.9 \times 10^{-4}\%$. As a rat weighing 330 Gm eats ca. 20 Gm of the diet a day, the estimated clonidine dose was ca. 300 $\mu\text{g}/\text{Kg}/\text{day}$.

From the First Department of Internal Medicine* and First Department of Pharmacology,** School of Medicine, Hokkaido University, Sapporo; Faculty of Pharmaceutical Sciences,*** University of Higashi Nippon Gakuen, Sapporo.

Results :

Regarding the tissue histamine content in SHR and WKY, endogenous histamine content in brainstem, heart, and kidneys was significantly increased in SHR at 8 weeks of age as compared with those of control WKY. However, at 18 weeks of age, no significant difference was observed in histamine content of brainstem, heart, and kidneys between SHR and WKY. Regarding catecholamine content of brainstem, heart, and adrenal glands, no significant difference was seen between SHR at 14 weeks of age and age matched WKY. However, the turnover rate of ^3H -norepinephrine tended to decrease in SHR as compared with WKY. In contrast, turnover rate of ^3H -norepinephrine in heart was increased in SHR as compared with WKY. One month administration of clonidine (300 $\mu\text{g}/\text{Kg}/\text{day}$ p.o.) produced hypotension, bradycardia, and weight loss. Therefore, clonidine at this dose was considered to be toxic. Regarding histamine content in SHR treated with clonidine for 1 month, insignificant increase was seen in brainstem, while no change of histamine content was seen in heart and kidneys. With regard to brainstem norepinephrine content, no significant difference was seen between clonidine administered group of SHR and control SHR under the same experimental conditions.

Discussion and Conclusion :

One of the most interesting observations in the present experiments was that endogenous histamine content of brainstem, heart, and kidneys in SHR at 8 weeks of age was significantly increased as compared with those of WKY. The tissue histamine content in SHR at 18 weeks of age showed no significant difference between SHR and age matched WKY. Therefore, it will be speculated that increase of histamine content in young SHR may be related to the initiation mechanism of hypertension under the consideration that the endogenous histamine is associated with the blood pressure regulation.