A Study Concerning the Methods of Medication for the Treatment of Hypertension. Hideaki Higashino, and Aritomo Suzuki. Department of Pharmacology, Kinki University School of Medicine, Osaka-fu 589.

Recently, long-acting antihypertensive drugs such as slow discharge forms of calcium blockers, β-blockers and ACE inhibitors have become to be used very frequently for the treatment of hypertensive patients by reason of simplicity of administration and persistently suppressing effect. Then, do long-acting antihypertensive drugs have superior pharmacological effects compared with the ordinary short-acting ones? From these concern, we have studied the differences in the pharmacological effects between two different ways of medication, short-acting and long-acting ways, using stroke-prone SHR (SHRSP).

The methods of medication to rats were settled as follows: For the purpose of short-acting medication, the drugs dissolved in 15% Arabic gum solution (ml/kg) were administered to rats with one shot in every morning by means of a gastric catheter. For the purpose of long-acting medication, the drugs mixed in powdered chow were fed chronically to rats as the same quantity per day as the former groups in two agents, prazosine and norphenephrine, in which the former is an anti-vasocontractile α1-antagonist and the latter is a vasocontractile α1-stimulator, were administered to 2- and 6-month-old SHRSP for 5 and 13 months, respectively.

When 0.1mg/kg prazosine was given to 6-month-old SHRSP with one shot by means of a gastric catheter, the blood pressure decreased by 10-20% more than 5 hours in duration, and heart rate increased conversely for 4 hours after administration of the drug, and then returned to the initial rate. When 1mg/kg norphenephrine was given to 6-month-old SHRSP with one shot, the blood pressure increased by a few percent for 3 hours and then decreased by 9%, and heart rate repeated up and down for 3.5 hours and then decreased by 2-10%. These physiological responses induced by two drugs were observed as somewhat weaker in 6-month-old SHRSP as observed in age-matched WKY. These findings represent that 6-month-old SHRSP still maintains a control mechanism through baroreceptor reflex, although it becomes weaker compared with WKY or younger SHRSP. In chronically drug administered experiment using 6-month-old SHRSP, both short-acting prazosine and norphenephrine administered groups were inhibited the elevation of blood pressure by 15-30% after second month of starting of this experiment. On the other hand, other two groups given by chow mixed with two different drugs couldn't show a significant decrease of blood pressure compared with control group. Moreover, both hypertensive (H) and sclerotic (S) changes of arteries in ocular fundus, which were determined by modified Scheie's classification, delayed prominently in short-acting norphenephrine treated groups during period of these observation compared with non-treated control and prazosine treated two groups. The average half life span after beginning of this experiment were as follows: 21.5, 23.5, 22.5, 36.0 and 23.0 weeks in control, short-acting prazosine, long-acting prazosine, short-acting norphenephrine, and long-acting norphenephrine treated groups, respectively. In chronically administered experiment using 2-month-old SHRSP, the changing course of blood pressure resembled to the results from 6-month-old SHRSP, but remarkable edema in their lower limbs were observed with high frequency (80%) after third month of medication as a adverse effect.

From above results, we concluded that 1) Long-acting medication of antihypertensive agents such as prazosine would not delay the development of hypertensive changes in the artery, and also prolong their life span. 2) Short-acting medication of drugs such as prazosine and even norphenephrine with completely opposite action to prazosine would inhibit further elevation of blood pressure with age. 3) It would be necessary to consider the physiologically homeostatic functions including a baroreceptor reflex system which readjust the disorders to the normal states even in the old hypertensive subjects, when we tried to treat the hypertensive patients using any suppressive agents.