22) The Therapeutic Effect of Several Anti-hypertensive Drugs and Diet on M-SHRSP——Changes in Life Spans, Blood Pressures, Plasma Hormones, Fundus Oculi and Internal Organs. (Second report) Yoshio Ohta, Hiroki Shiokawa, Taka-aki Chikugo, Nobuko Morita, Yoh Hamada, Kozo Okamoto. Department of Pathology, Kinki University School of Medicine, Osaka 589, Faculty of Home Economics, Kobe Women's University, Kobe 654, Department of Ophthalmology, Tondabayashi Hospital, Osaka 584.

Introduction:

Using M-SHRSP, which seem to be a useful animal model for studying human juvenile malignant hypertension, we have conducted a study in order to secure data on the prevention of and therapy for malignant hypertension. A portion of these results have been reported previously (Morita et al.: Jpn. Heart J. 29: 575, 1988; Ohta et al.: Jpn. Heart J. 30: 543-545, 1989). Further observations were obtained in this study.

Materials and methods:

Only male M-SHRSP were used. Drugs employed were captopril and SQ 29852 (obtained from SQUIBB JAPAN, INC.), both mixed in food, 30-40 mg/kg/day; and hydralazine hydrochloride (obtained from CIBA-GEIGY JAPAN), mixed in drinking water, 60-80 mg/l. A special 33% fish meal diet (crude protein ca. 23%) was also prepared. These drugs and the diet were given either separately or in combinations of two or three, beginning at weaning, maturity or adulthood. Control rats were fed a stock chow diet (Funabashi SP) and given tap water ad libitum. Blood pressures were measured using the photoelectric volume oscillographic method without anesthesia. Retinal vessels were observed with a funduscope (Kowa RC2). Plasma renin and aldosterone concentrations were measured through radioimmunoassay. All of the animals were autopsied and pathologically examined following natural death or sacrifice.

Results and Discussion:

Compared to the control rats, a preventative and/or an antihypertensive effect was found for individual treatment with SQ 29852, captopril, hydralazine or 33% fish meal diet, in that order of effectiveness. Through suitable diet appropriately combined with administration of these antihypertensive agents, each involving different mechanisms, anti-hypertensive effects were strengthened over those of individual treatments. These effects were in the same order as above. Comparing the three different stages for starting treatment, greater effects in both suppression of the development of hypertension and in decreasing blood pressures were found in the order of weaning, maturity and adulthood. This seems to indicate that the earlier the treatment starts, the greater the effect. It is possible to lower the blood pressures of M-SHRSP to within normal ranges at any stage of life through a combination of captopril or SQ 29852, hydralazine and a fish meal diet. But weight gains were suppressed under these treatments. On the other hand, for M-SHRSP treated with hydralazine in combination with either captopril or SQ 29852, but with no change in diet, blood pressures remained around 150 mmHg and weights were not suppressed. Furthermore, none of the rats in this group evidenced any cerebrovascular lesions. This combination seems one of the best therapies for M-SHRSP. For M-SHRSP, treatment with either captopril or SQ 29852, separately, suppresses the occurrence of hypertensive vascular lesions (especially angionecrosis) in a variety organs other than the testes and greatly prolongs life spans, even though these rats continue to maintain stable moderately or significantly high blood pressures. From these results, we therefore set forth the hypotheses that there is a possibility that in malignant hypertension, factors other than high blood pressure itself, but factors which interact with its effects, play a role in the occurrence of such hypertensive vascular lesions as angionecrosis. Further, that captopril and/or SQ 29852 have the potential to suppress such factors and therefore prevent and/or repair hypertensive vascular lesions, plus, subsequently, greatly lengthening life spans.