44) Effect of One of Antithrombotic Drugs on the Development of Stroke in SHRSP. Ryoichi Horie, Takehiro Igawa, and Yukio Yamori. Department of Pathology, Shimane Medical University, Izumo 693.

INTRODUCTION

As is well known, stroke-prone spontaneously hypertensive rats (SHRSP) develop commonly arterionecro-thrombogenic stroke. In the present study, the effect of one of antithrombotic drugs - Cilostazol - on the development of stroke was investigated, based on the previous report that Cilostazol was evaluated as an antithrombotic drug by determining its inhibitory effect on platelet aggregation induced by various aggregating agents in experimental models and in humans in vitro (KIMURA ET AL.: DRUG RES 35: 1144, 1985).

MATERIALS AND METHODS

Used rats were 40 female SHRSP (A₃, A₁-sb and A₄ strain, F₅₆₋₅₇) maintained at WHO Collaborating Center for Research on Primary Prevention of Cardiovascular Diseases (Izumo, Japan). At the age of 100 days after birth, these rats were divided into two groups. One group was fed on Oriental MF diet containing 600 ppm Cilostazol (6-[4-(1-cyclohexyl-1H-tetrazol-5-yl)butoxyl]-3, 4-dihydro-2(1H)-guinolone) and the other group was fed on Oriental MF diet as a control. Blood pressure (Tail-pulse pickup method), body weight and neurological deficits were repeatedly checked until 500 days after birth and at the time survived rats were sacrificed. Autopsy was performed for further pathohistological examinations in both natural death cases and sacrificed ones.

RESULTS

(1) In the Cilostazol-treated group, stroke incidence (1/20) was significantly lower than that in the control group (6/20) ($p < 0.01$), while average life span (430 ± 22 days, $M \pm SE$), developmental course of hypertension (e.g. 203 ± 4 mmHg, 300 days after birth) and body weight (e.g. 231 ± 4 g, 300 days after birth) in Cilostazol-treated group had not significant differences from controls (411 ± 25 days, 199 ± 4 mmHg, 228 ± 4 g), respectively.

(2) On the histological findings of 6 stroke death cases in control groups were all cerebral infarction caused by arterionecro-thrombosis. Stroke lesions were localized in left and/or bilateral occipitoparietal regions (brain weight: 2.10 ± 0.07 g, $M \pm SE$). In contrast to that, one case in Cilostazol-treated group showed small hemorrhagic infarction in the left occipital region. Average brain weights in the cases which did not develop stroke were 1.83 ± 0.05 g in control group and 1.88 ± 0.03 g in Cilostazol-treated group, respectively.

(3) Average plasma Cilostazol level during the period of experiment was 815.43 ± 96.67 ng/ml which corresponded approximately to that during p.o. administration of 20 mg/kg/day Cilostazol as previously reported (AKIYAMA ET AL.: DRUG RES 35:1124, 1985).

CONCLUSION AND DISCUSSION

Previously the preventive effect of antithrombotic agent on stroke in SHRSP was reported (YAMORI ET AL.: In PROPHYLACTIC APPROACH TO HYPERTENSIVE DISEASES: 573, RAVEN PRESS 1979). The present study demonstrated that Cilostazol prevented arterionecro-thrombogenic stroke in female SHRSP (F₅₆₋₅₇) probably due to its inhibitory effect on thrombosis, although the effect of Cilostazol on platelet aggregation in this pathological animal model (SHRSP) should be reconfirmed.