39) Effects of Antihypertensive Treatments on Ocular Lesions of Streptozotocin-Induced Diabetes Mellitus in Spontaneously Hypertensive Rats. Atsuko Miyazawa*, Hiroyuki Shimizu*, Miho Kusaka**, Koichiro Kishi**, and Hirofumi Sokabe**, Departments of *Ophthalmology and **Pharmacology, Jichi Medical School, Tochigi-ken 329-04.

SUMMARY Effects of antihypertensive treatments on ocular lesions were evaluated in spontaneously hypertensive (SHR) rats with streptozotocin (STZ)-induced diabetes mellitus. STZ treatment induced ocular lesions such as narrowing of retinal arterioles, caliber irregularity, papilledema and cataracta in these rats. Enalapril, ramipril and arotinolol decreased blood pressure (BP) and prevented the progress of ocular lesions. Nisoldipine tended to decrease blood glucose (BG) and prevented the progress of ocular lesions. Therefore, antihypertensive treatments were shown to be effective in preventing the progress of ocular lesions in hypertensive rats with diabetes mellitus. Hypertension, as well as high BG, was suggested to play an important role in inducing ocular lesions.

INTRODUCTION Recent clinical reports indicated that hypertension accelerates diabetic nephro- and retinopathies, whereas antihypertensive treatments may retard them. We have reported preventive effects of antihypertensive treatments on renal lesions of STZ-induced diabetes mellitus in SHR rats. In this study, effects of antihypertensive treatments on ocular lesions of these rats were examined.

MATERIALS AND METHODS Six groups of 12-week-old SHR rats, 9-13 rats in each, from the colony of the Department of Pharmacology, Jichi Medical School, were used. After the surgery of unilateral nephrectomy and an overnight fast, 5 groups of rats were treated with 30 mg/kg of STZ intravenously via the dorsal tail vein. These rats were treated with following 4 antihypertensive drugs orally for 12 weeks thereafter: arotinolol, a β -adrenoceptor blocking drug (20 mg/kg per day); nisoldipine, a calcium entry blocking drug (3 mg/kg per day); enalapril and ramipril, angiotensin I converting enzyme inhibitors (10 and 1 mg/kg per day, respectively). Body weight (BW), heart rate (HR), tail BP were determined every week. BG was determined biweekly. Retinal lesions and cataracta were observed, and photographs of the fundi were taken several times in the experiment. Narrowing of retinal arterioles, caliber irregularity, papilledema and cataracta were graded into 4 steps, respectively. At the end of the experiment, mean BP was determined directly without anesthesia or restraint through a cannula inserted into the abdominal aorta. Then the rats were sacrificed, and the retina was fixed with 10 % formalin, and embedded in paraffin. Thin sections were stained with hematoxylin-eosin, and examined microscopically.

RESULTS STZ treatment induced chronic hyperglycemia (300-400 mg/dl), decreased BW and HR, and increased ocular lesions. Changes of the retina, such as narrowing of arterioles, caliber irregularity and papilledema, and changes of the lens, such as cataracta, were observed. In the microscopic examination, edematous swelling in the nerve fiber layer of the retina and degeneration of ganglion cells were observed. Enalapril, ramipril and arotinolol decreased BP and prevented the progress of ocular lesions. Nisoldipine tended to decrease BG, and prevented the decrease of BW and the progress of ocular lesions.

DISCUSSION Ocular lesions of SHR rats were advanced by STZ-induced diabetes mellitus. Normalization of BP by antihypertensive treatments prevented the progress of these ocular lesions. Ocular lesions were prevented largely by nisoldipine treatment, which tended to decrease BG in this study. Therefore, high BG and hypertension were suggested to play important roles in inducing ocular lesions in SHR rats with STZ-induced diabetes mellitus.