62) Gonadectomy modulate the action of antihypertensive agents in spontaneously hypertensive rats. Yoshiko Masubuchi, Toshio Kumai, Taiichiro Ohno, Masami Tanaka and Masanao Hirai. Department of Pharmacology, St. Marianna University School of Medicine, Kawasaki, Kanagawa 213

We have previously reported that (1) regenerated adrenal gland in the presence or absence of gonad increases significantly systolic blood pressure (BP) in both spontaneously hypertension rat (SHR) and Wistar Kyoto normotensive rats (WKY), (2) gonadectomy significantly retards BP both in regenerated adrenal bearing and intact SHR, (3) gonadectomy did not alter the BP in WKY. These indicates that gonadal hormones play of important role in the pathogenesis of essential hypertension.

The present work extends our earlier study on the gonadectomy-reduced spontaneous hypertensive and elucidates the sites whereby gonadectomy exert its inhibitory effects upon spontaneous hypertension by using antihypertensive agents which had known action-mechanisms. SHR originated from WKY male and female were used in this work. All animals were kept in our Research Animal Bulding where temperature ($23\pm1^{\circ}\text{C}$), humidity ($55\pm5\%$) and lighting (06:00-18:00) were controlled for 24 hours, and supplied with water and regular commercial rat chow (CLEA-CE-2) which has a relatively low fat content (less than 3.8%) ad libitum. The animals were gonadectomized at 4 weeks old and daily BP measurements were taken for consecutive days before and after the operation by tail-cuff method using a programmed pressure transducer, digital panel, heart rate meter and rat housings with heating bases (Natsume-KN-209) in consious rats. Animals treated one of 6 antihypertensive drugs, these were captopril (5mg/kg,i.p.) as an angiotensin converting enzyme inhibitor, nifedipine (150 $\mu\text{g/kg,i.p.}$) as a calucium-antagonist, prazosin (30 $\mu\text{g/kg,i.p.}$) as an α_1 -receptor blocker, clonidine (20 $\mu\text{g/kg,i.p.}$) as an α_2 -receptor agonist, propranolol (5mg/kg,i.p.) as a β -receptor blocker and spironolactone (50mg/kg,i.p.) as an aldosterone antagonist. Captopril significant lowered BP in intact SHR but not changed in castrated SHR, where ΔBP (ratio of blood pressure in treated to pretreated rats) was significantly different (intact >castrated SHR) and increased ΔH (ratio of heart rate in treated to pretreated rats) was not different among the intact and castrated SHR. Nifedipine significantly lowered BP both in intact and castrated SHR, where ΔBP was not different among these animals however, ΔH was significantly different in castrated groups but not different in intact animals. Prazosin significantly lowered BP both in intact and castrated animals, where ΔBP was significantly different (castrated > intact SHR) although ΔH was not different among these groups. Clonidine significantly reduced BP in intact animals, opposingly, a significantly elevation was shown in castrated animals where ΔBP and ΔH were significantly higher in castrated group than those of intact group. Propranolol produced significantly decrease BP in intact group but unaltered in castrated animals, where ΔBP was significantly different (intact >castrated SHR) and ΔH was unaltered. Spironolactone significantly lowered BP in intact animals but not changed in castrated animals, where ΔBP and ΔH were not different among these two groups.

These findings underscored our hypothesis that the etiology of spontaneous hypertension in SHR is mediated not only by hemodynamic factors but also by abnormal activity of the hypothalamic-pituitary-gonadal axis. Present results indicate that actions of antihypertensive drugs involvment in reduction on hypertensive BP disappear coincident with the removal of gonad, such as captopril, propranolol and spironolactone, further, elevating effects on BP of clonidine was appeared and unusual drop in BP of prazosin was induced by the castration. These findings therefore raise the possibility that mechanisms of action of antihypertensive drugs is serially involved in mediating the regulatory influence of gonadal function (sex hormones).

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