Inhibition of Hypertension and Organ Changes under Long-Term Administration of Anti- Hypertensive Drugs to SHR

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This experiment aims to know how much organ damages could be inhibited, when anti-hypertensive drugs are administered for a long term to SHR of pre-hypertensive stage.

Method:

Male SHRs, 5 weeks of age, were orally administered fusaric acid (DBH inhibitor) 150 mg/Kg/day, hydralazine 30 mg/Kg/day, and propranolol 30 mg/Kg/day, which were mixed with normal laboratory powdered stock diet (containing protein 24.2%, fat 5.5%, sodium 0.24%, and calcium 1.76%) and were dried to be solid overnight under 40°C. Changes of blood pressure and body weight were checked frequently and organ changes were examined microscopically at the age of 10 weeks and 15 weeks (5 weeks and 10 weeks after the beginning administration of anti-hypertensive drugs, respectively). Non-treated SHRs at the same age were used as controls.

Results:

1. Changes of body weight; 80–85 Gm at 5 weeks of age, 145–152 Gm at 10 weeks, and 198–220 Gm at 15 weeks, which show no difference between treated SHR groups and non-treated ones.

2. Changes of blood pressure; The mean of blood pressure was 105.9 mmHg at pre-hypertensive stage, 5 weeks of age. At 10 weeks of age, significant changes were observed; blood pressure of control group raised to 151 mmHg, that of fusaric acid group was 116 mmHg, hydralazine group was 132 mmHg, and propranolol group was 135 mmHg. At 15 weeks of age, more significant changes were obtained; hypertension was completely inhibited in fusaric acid and hydralazine groups (120 mmHg and 132 mmHg, respectively) but hypertension was developed in propranolol group (160 mmHg) and control group (161 mmHg).

3. Changes of heart and kidney weight; There was no significant difference of weight among these groups at 10 weeks or 15 weeks of age.

4. Microscopic organ changes; Organ changes are summarized on the table.

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	Kidney			
	Interlobular Arteries		Arcuate Artery	
	Perinuclear Vacuolation 10 w → 15 w	Medial Thickening 10 w → 15 w	Perinuclear Vacuolation 10 w → 15 w	Medial Thickening 10 w → 15 w
Control	+ ~ ++ → - ~ +	++ → ++ ~ ###	- → ±	- → ++ ~ ###
Fusaric Acid	± ~ + → ± ~ +	+ → ± ~ +	- → +	- → ±
Hydralazine	+ → ± ~ +	± ~ + → + ~ ++	- → +	± → ± ~ +
Propranolol	+ → - ~ ±	± ~ + → +	- → +	- → + ~ ++
	Heart			
	Hypertrophy of Cardiac Muscle 10 w → 15 w	Intra-myocardial Branch of Coronary Artery		
		Perinuclear Vacuolation 10 w → 15 w	Medial Thickening 10 w → 15 w	
Control	+ ~ ++ → + ~ ++	± → +	- ~ + → +	
Fusaric Acid	- → ±	+ → ± ~ +	- ~ ± → ± ~ +	
Hydralazine	+ → ±	+ → +	+ → ± ~ +	
Propranolol	± → ± ~ +	+ → ± ~ +	± ~ + → +	

(Hematoxylin-Eosin staining)

Discussion :

Hypertension was completely inhibited after administration of fusaric acid and hydralazine. Fusaric acid showed stronger inhibitory effect than hydralazine. Hypertension was developed in SHR at 15 weeks of age after administration of propranolol.

Microscopically, perinuclear vacuolation and medial thickening in interlobular and arcuate arteries were observed in control (non-treated) group. And lesser perinuclear vacuolation and stronger medial thickening were also observed with aging, which means that such functional changes as vascular contraction might gradually turn into organic wall thickening.

In fusaric acid group, changes of interlobular and arcuate arteries were slight, but in hydralazine group medial thickening of interlobular arteries was observed to be moderate although hypertension was inhibited. Such humoral factors as catecholamines and renin, which were not inhibited by administration of hydralazine, could make further arteriolar changes as vasculotoxic.

In propranolol group, medial thickening of arcuate arteries was moderate, which expresses adaptation for hypertension that would be produced by relatively dominant state of α -adrenergic receptors after administration of β -adrenergic blockers.

Microscopic changes of heart have become more remarkable in control group; hypertrophy of cardiac muscle, perinuclear vacuolation, and medial thickening of intra-myocardial branch of coronary artery. But no significant change was developed in all these treated groups.