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Cardiac Output in Conscious One-clip, Two-kidney Renovascular Hypertensive Rats*)

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ABSTRACT

Cardiac output and arterial pressure in the conscious state were observed in one-clip, two-kidney renovascular hypertensive rats with a chronically implanted electromagnetic flow probe and an arterial cannula. Normal Wistar rats were used as controls. At rest, cardiac output per body weight did not show any difference between hypertensive rats and normal controls. This kind of experimental hypertension was maintained entirely by elevation of total peripheral resistance. In transposition response induced by tranposing rats from their home cage to a new cage, after beta adrenoceptor blockade with propranolol, total peripheral resistance remained unchanged in contrast to control rats in which resistance was elevated. This may be due to either a less marked vasoconstriction in the splanchnic area or a greater non-beta adrenergic vasodilatation in the skeletal muscle in transposition response in hypertensive rats than in control rats.

INTRODUCTION

In a previous study cardiac output was measured in conscious spontaneously hypertensive rats (SHR) by means of an electromagnetic flow probe chronically implanted around the ascending aorta[3]. The total pooled data showed that the cardiac index was significantly higher than the corresponding value in normal control rats. However, the arterial pressure in probe implanted SHR was significantly lower than that in SHR without probe. It was assumed that probe implantation or implanted probe itself in some way lowered the arterial pressure, which, being a decrease in afterload, secondarily induced an increase in cardiac output. Without aortic probe, the cardiac index in SHR was estimated to be within the normal range[2].

It is of interest to observe whether aortic probe implantation also induces a lowering of arterial pressure and assumed secondary increase in cardiac output in other kinds of hypertensive rats. Thus, cardiac output was measured in one-clip, two-kidney renovascular hypertensive rats in the present study. This particular kind of hypertension was selected because its hemodynamic data were thought to be especially meager. Unlike the hypertension in SHR, the hypertension in one-clip, two-kidney renovascular hypertensive rats was stable and a considerably high pressure level was maintained even after aortic probe implantation.

METHODS

Male Wistar rats at about 10 weeks of age were anesthetized by intraperitoneal injection of thiamylal sodium at a dose of 50 mg/kg. In order to prepare one-clip, two-kidney renovascular hypertensive rats, the left renal artery was reached retroperitoneally by a flank incision and a clip made from a metal tape, 1 mm wide by 0.1 mm thick, with a gap of 0.2 mm, was placed on it. Two to three weeks thereafter, rats were anesthetized again to implant an aortic flow probe and an arterial cannula by the method described previously[4]. Normal Wistar rats of similar age were used as controls.

Each implanted rat was kept in isolation in a polyethylene box cage containing wood chips

*) 寺西泰弘，入内島十郎：無麻酔1-クリップ，2-腎性 腎血管性高血圧ラットの心拍出量

and recordings were usually made with the rat remaining in the cage.

Transposition response[4] is an excited state of the rat's cardiovascular system by activation of the sympathoadrenal system, induced by transposing rats from their home cage to a new cage. This response was employed to study the possible difference in the cardiovascular control system between hypertensive rats and normal rats.

For statistical analysis, the student's t-test for group or paired data was used throughout. P values of <0.05 were considered to indicate statistical significance.

RESULTS

Hemodynamic parameters at rest

One example each of simultaneous recording of aortic flow and arterial prssure in conscious renovascular hypertensive and normal control rats at rest is presented in Fig. 1. The mean cardiovascular parameters with SD from several hypertensive and normal rats are tabulated in Table 1.

Arterial pressure, total peripheral resistance index and cardiac work index were singnificantly higher in hypertensive rats than in controls, while heart rate and cardiac index did not differ between the two groups.

In a different series of experiment, arterial cannulation without probe implantation was performed in 14 renovascular hypertensive rats and 13 normal controls. The mean arterial pressure with SD in the conscious state was 171 ± 15.8 mmHg in hypertensive rats and 110 ± 6.05 mmHg in control rats. These were not significantly different from the respective corresponding values in the probe implanted hypertensive and normal rats.

Transposition response in renovascular hypertensive rats

One example of recording of aortic flow and pressure before and during transposition respone is presented Fig. 2. The mean cardiovascular parameters$\pm$SD from 5 hypertensive rats before and during the response are tabulated

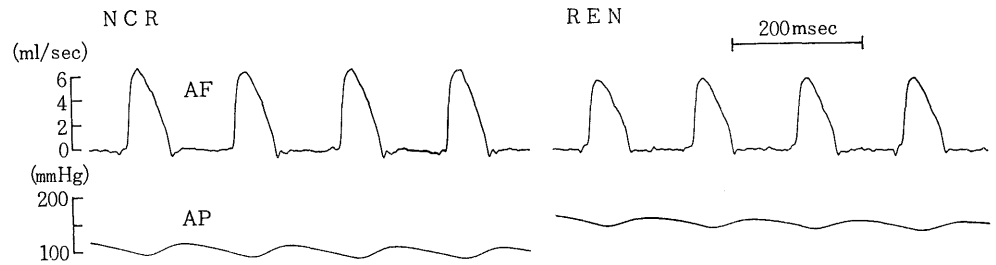

Fig. 1. Simultaneous recording of aortic flow (AF) and arterial pressure (AP) in a conscious normotensive control rat (left, NCR) and one-clip, two-kidney renovascular hypertensive rat (right, REN) at rest.

Table 1. Comparison of cardiovascular parameters at rest between one-clip, two-kidney renovascular hypertensive rats (REN) and normotensive control rats (NCR)

	REN	NCR	P<
Arterial pressure (mmHg)	161±25.6	110±8.18	0.001
Heart rate (beats/min)	384±22.4	358±34.6	NS
Cadiac index (ml/min/100 g)	22.7±3.24	22.5±2.17	NS
Total peripheral resistance index (mmHg/ml/min/100 g)	7.29±1.83	4.94±0.57	0.001
Cardiac work index (mmHg · ml/min/100 g)	3630±600	2490±311	0.001
n	11	8	
male/female ratio	10/1	7/1	
body weight (g)	281±31.1	307±52.1	
age (week-old)	13.6±1.43	13.1±2.47	
days after implantation	3.18±0.83	4.25±1.79	

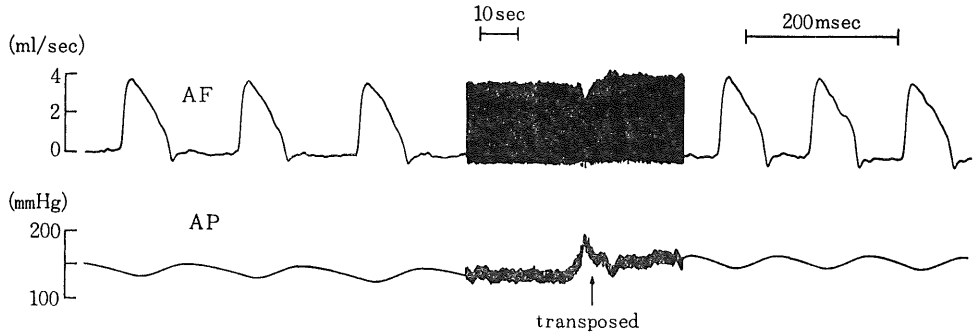

Fig. 2. Changes in aortic flow (AF) and arterial pressure (AP) in a one-clip, two-kidney renovascular hypertensive rat in transposition response.

Table 2. Comparison of parameters before and during transposition response in one-clip, two-kidney renovascular hypertensive rats

	before	during	P<
Arterial pressure (mmHg)	172±23.9	181±21.6	0.1
Heart rate (beats/min)	404±12.2	473±39.1	0.02
Cardiac index (ml/min/100 g)	25.1±4.05	32.8±6.20	0.02
Total peripheral resistance index (mmHg/ml/min/100 g)	7.16±2.15	5.77±1.44	0.1
Cardiac work index (mmHg·ml/min/100 g)	4256±443	5861±806	0.01

n=5 (all male); body weight: 297±36.9; 14.3±1.54 week-old; 2.80±0.40 days after implantation

in Table 2. Heart rate, cardiac index and cardiac work index were increased significantly in the response. The changes in arterial pressure and total peripheral resistance were insignificant. In the same group of hypertensive rats, induction of transposition response was repeated after beta adrenoceptor blockade with propranolol (1 mg/kg, i. p.). The changes in hemodynamic parameters by the blockade are presented in Fig. 3. By the blockade, cardiac output was decreased and total peripheral resistance was increased significantly. In transposition response cardiac output was still increased significantly after the blockade (Table 3). The increase in arterial pressure was still insignificant ($p<0.1$) and the total peripheral resistance remained almost unchanged.

DISCUSSION

The hypertension in one-clip, two-kidney renovascular hypertensive rats was found to be maintained by an elevation of total peripheral resistance with normal cardiac output. In this respect, one-clip, two-kidney hypertensive rats were similar to two-clip, two-kidney rats in which normalcy of cardiac output has been observed by Ferrone et al.[1]. In one-clip, one-kidney renovascular hypertensive rats, however, a slight increase in cardiac output has been reported[5].

Unlike the hypertension of SHR[8], one-clip, two-kidney renovascular hypertension was so stable that the arterial pressure level was almost unaffected by the intervention of aortic probe implantation.

Transposition response was variable in different hypertensive rats: arterial pressure remained almost unchanged in the response in normal rats and one-clip, one-kidney renovascular hypertensive rats and was elevated in SHR, DOCA salt hypertensive rats and neurogenic hypertensive rats[6]. In the present study the arterial pressure tended to increase slightly in the response in one-clip, two-kidney renovascular hypertensive rats ($p<0.1$).

After beta blockade, the increase in arterial pressure in transposition response was insignificant in contrast to normal rats, in which a marked increase in arterial pressure was observed. Cardiac output was still increased in transposition response in renovascular hypertensive rats. This parameter remained un-

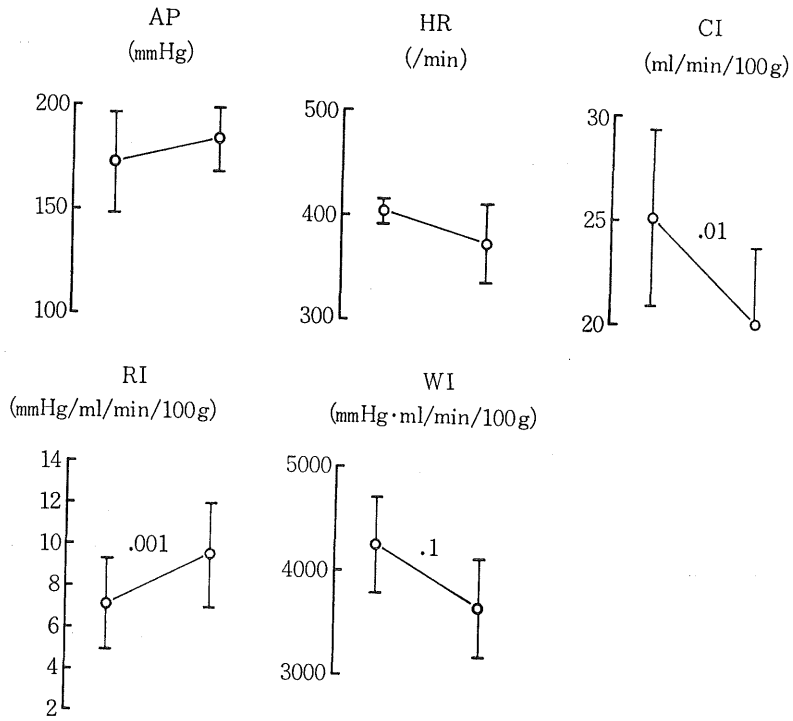

Fig. 3. Changes in cardiovascular parameters in one-clip, two-kidney renovascular hypertensive rats by beta blockade (propranolol, 1 mg/kg, i. p., after 30 min). Note that cardiac index (CI) was decreased and total peripheral resistance (RI) increased. AP: arterial pressure, HR: heart rate, WI: external cardiac work index. mean±SD, n=5.

Table 3. Comparison of parameters before and during transposition response in one-clip, two-kidney renovascular hypertensive rats 30 min after propranolol (1 mg/kg. i. p.).

	before	during	P<
Arterial pressure (mmHg)	184±15.1	203±9.62	0.1
Heart rate (beats/min)	377±34.6	405±47.0	N S
Cardiac indsx (ml/min/100 g)	20.1±3.68	22.1±4.37	0.02
Total peripheral resistance index (mmHg/ml/min/100 g)	9.57±2.49	9.48±1.70	N S
Cardiac work index (mmHg·ml/min/100 g)	3643±480	4485±967	0.05

changed in normal rats after beta blockade. Total peripheral resistance, which was increased in transposition response after beta blockade in normal rats[4], remained almost unchanged in one-clip, two-kidney hypertensive rats. This may be due to either less marked vasoconstriction in splanchnic area or greater non-beta adrenergic vasodilatation in skeletal muscle in transposition response in hypertensive rats than in control rats. Peripheral flow measurement would clarify this point. Qualitatively, similar phenomena have been observed in SHR: After beta blockade, cardiac output was still increased in transposition response more markedly than in renovascular hypertensive rats and the change in total peripheral resistance was insignificant[3].

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