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DEVELOPMENT OF HEART FAILURE FOLLOWING TRANSVALVULAR CATHETERIZATION OF THE LEFT VENTRICLE IN SPONTANEOUSLY HYPERTENSIVE RATS

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Systemic hypertension is one of the main etiological factors in the development of congestive heart failure [4]. Pfeffer et al. [8] showed that the cardiac output of spontaneously hypertensive rats (SHR) is lower at the age of 25 weeks than at 13 weeks. However, these data were obtained under acute experimental conditions, which may have differed in their effect on the circulatory system of animals of different ages [11].

The aim of this investigation was to compare systemic hemodynamic parameters in unanesthetized SHR and normotensive rats (NTR) of different ages, by the method of radioisotope-labeled microspheres.

EXPERIMENTAL METHOD

Experiments were carried out on SHR (of the Okamoto—Aoki line, from the Heidelberg University colony, West Germany) and Wistar—Kyoto NTR. An arterial catheter was implanted in the abdominal aorta through the femoral artery. After 1-2 days, under pentobarbital (40 mg/kg) or ether anesthesia, the left ventricle was catheterized through the right carotid artery. In one series of experiments the left atrium was catheterized. To do so, under artificial respiration and under open chest conditions a catheter was introduced into the auricle of the left atrium. The peripheral ends of the catheters were brought out on the animal's back and fixed in the interscapular region. The hemodynamic parameters were studied by the use of radioactive isotope-labeled microspheres [1]. The cardiac catheter (located in the left ventricle or left atrium) was used to inject the microspheres, the arterial catheter to take blood and

TABLE 1. Hemodynamic Parameters in 5-month-old NTR and SHR 3 and 24 h after Catheterization of Left Ventricle under Pentobarbital Anesthesia

Parameter	Time after operation, h	NTR ($n=5$)	SHR ($n=6$)
Mean BP, mm Hg	3	123±4	171±5*
	24	100±7	138±9*
HR, min^{-1}	3	300±16	315±10
	24	312±15	315±13
CI, ml/min/100 g	3	31,3±4,0	26,6±2,3
	24	32,6±3,4	29,1±2,7
TPVR, mm Hg/ml/min 100 g	3	4,22±0,54	6,58±0,38
	24	3,18±0,39	4,85±0,33

Legend. *$p < 0.05$ compared with corresponding value for NTR.

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TABLE 2. Hemodynamic Parameters in 10-month-old NTR and SHR 3 h after Catheterization of Left Ventricle under Pentobarbital or Ether Anesthesia

Parameter	Pentobarbital anesthesia		Ether anesthesia
	NTR ($n=6$)	SHR ($n=5$)	SHR ($n=6$)
Mean BP, mm Hg	125±4	184±9*	205±5
HR, min^{-1}	355±16	348±35	340±13
CI, ml/min/100 g	27,0±2,3	12,9±2,5*	29,3±1,8**
TPVR, mm Hg/ml/min/100 g	4,73±0,28	12,27±2,74*	7,12±0,41**

Legend. *p < 0.05 compared with corresponding value for NTR. **p < 0.05 compared with corresponding value for SHR undergoing operation under pentobarbital anesthesia.

TABLE 3. Hemodynamic Parameters in 10-month-old SHR 24 h after Catheterization of Left Ventricle under Ether Anesthesia and after Catheterization of Left Atrium under Pentobarbital Anesthesia

Parameter	Catheterization of left ventricle (n = 8)	Catheterization of left atrium (n = 4)
Mean BP, mm Hg	132±9	168±15
HR, min^{-1}	295±30	428±18*
CI, ml/min/100 g	17,6±1,6	28,6±4,0*
TPVR, mm Hg/ml/min/100 g	8,08±1,02	6,60±1,81

Legend. *p < 0.05 compared with corresponding value for catheterization of left ventricle.

to record the blood pressure (BP). The number of microspheres was determined with a "Compugamma" gamma-counter (LKB — Wallac, Finland). The cardiac output was calculated by means of standard equations [3].

The results were subjected to statistical analysis by Student's t tests for paired and unpaired samples. The data are presented in the form $\bar{X} \pm m$.

EXPERIMENTAL RESULTS

In SHR aged 5 months BP 3 h after catheterization of the left ventricle under pentobarbital anesthesia remained higher than in NTR, and the total peripheral vascular resistance (TPVR) remained increased, whereas the cardiac index (CI) and the heart rate (HR) of these two groups of animals did not differ. Similar results were obtained 24 h after the operation (Table 1). Values of parameters of the systemic hemodynamics determined in this investigation on SHR and NTR aged 5 months were close to those described in the literature [5, 7, 9, 10].

Transvalvular catheterization of the left ventricle under pentobarbital anesthesia led to a sharp fall of CI and a rise of TPVR in 10-month-old SHR as early as 3 h after the operation, compared with these parameters in NTR of the same age (Table 2), and in most cases the animals died on the 1st day after the operation.

In the series of experiments in which ether anesthesia was used transvalvular catheterization of the left ventricle also led to the development of heart failure, but more slowly. CI 6 h after the operation was 20% lower than 3 h after the operation, and 38% lower than 24 h thereafter (Table 3). These results show that pentobarbital causes a much more rapid development of heart failure, evidently due to its depressive action on the myocardium [6].

To study the possible mechanism of the rapid development of heart failure a series of experiments was carried out in which a catheter was introduced into the left atrium, through

which microspheres could be injected. The parameters of the hemodynamics 24 h after this operation in 10-month-old SHR differed essentially from data obtained 24 h after catheterization of the left ventricle (Table 3) and they were close to the values of these parameters studied in 5-month-old SHR and 5- and 10-month-old NTR (Tables 1 and 2).

The results thus show that no significant change takes place in the parameters of the systemic hemodynamics in SHR between the ages of 5 and 10 months, but the reserve capacity of the cardiovascular system is significantly reduced. This is manifested, for example, in the development of heart failure after transvalvular catheterization of the left ventricle, evidently due to a process of proliferation of connective tissue in the myocardium of SHR [2], which reduces the elasticity of the valve cusps and disturbs valvular function even when a thin polyethylene tube (external diameter 0.61 mm) is passed through it.

Considering that the development of heart failure in 10-month-old SHR takes place against the background of preceding prolonged hypertension, this model may be used to study the mechanisms of action and in the search for cardiotonic drugs.

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