Characteristics of Circadian Rhythm of Blood Pressure during Long-Term Hypertension Development in SHR Rats

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The specific features of circadian rhythm of BP were investigated in freely moving male SHR rats using telemetry monitoring technique. BP was recorded in the abdominal aorta according to 24-h/4-month schedule. The data were obtained from 22, 26, 30, 34, and 38-week-old animals. Normotensive Wistar rats (22 weeks) served as the control. It was found that the mean 24-h, daytime, and nighttime systolic and diastolic BP in hypertensive rats significantly surpassed the control throughout the observation period and practically did not change during prolonged hypertension. Some prognostically negative changes in the circadian rhythm of the basic hemodynamics system parameters appeared with time. For instance, the maximum 24-h systolic BP significantly increased in comparison with the initial level.

Key Words: *blood pressure; circadian index; circadian rhythm; telemetry monitoring; SHR rats*

The prognosis of arterial hypertension of various geneses depends on BP level and daily circadian rhythm of BP. For instance, the absence of significant difference between daytime and nighttime BP during pregnancy, secondary hypertension, diabetes mellitus, and other conditions correlates with the frequency of complication in target organs [1]. On the contrary, in accordance to F. Halberg conception, one of the main of vascular variability disorders (VVD) the circadian hyper-amplitude-tension (CHAT) is a "premetabolic syndrome" including prediabetes and prehypertension [2,4] and increasing the risk of cerebral stroke development [3]. It can be hypothesized that the development of hypertension is associated with the changes in circadian rhythm of cardiovascular system parameters. However, monitoring of the dynamics for circadian rhythm of cardiovascular system during hypertension development seems to be difficult in clinical practice, because it requires many-year BP monitoring in the same patients.

Here we studied the circadian profile of BP at various terms of hypertension in rats using telemetry monitoring technique. The significance of this method was confirmed by previous experiments [5-7].

MATERIALS AND METHODS

Experiments were performed on male SHR rats (spontaneously hypertensive rats; n=5) and Wistar rats (control group, n=5). Animal care and all manipulation were conducted in accordance to the Direction of the Ministry of Health of the USSR No. 755 (12.08.1977). Continuous telemetry monitoring of BP on Data Sciences International equipment was performed in Wistar rats once at the age of 22 weeks and in SHR rats starting from the age of 22 weeks for 4 months. Radio transmitters were implanted in rats during surgical procedure under general anesthesia. These devices continuously measured BP in the abdominal aorta, the data were wirelessly transmitted (radio signal) to a sensing device, and BP curves were saved in computer memory. Recordings were started 3 weeks after surgery. During monitoring, each animal was housed in individual cage with artificial light/dark cycle (7.00-19.00, lightness; 19.00-7.00, darkness). The obtained data were processed using Dataquest A.R.T.4.2 Gold software. The following parameters were recorded in

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rats of the control and treatment (at the age of 22, 26, 30, 34, and 36 weeks) groups: mean 24-h systolic (SBP) and diastolic (DBP) pressure, mean daytime and nighttime SBP and DBP, circadian index of SBP and DBP, and maximum and minimum 24-h SBP and DBP (SBP_{max}, SBP_{min}, DBP_{max}, and DBP_{min}). The mean and error of the mean were calculated. The data were treated using Student's *t* test. The differences were significant at $p \leq 0.05$.

RESULTS

24-h SBP and DBP were higher in spontaneously hypertensive rats at all terms of experiment than in normotensive animals (Table 1). These parameters tended to increase in SHR rats 1 month after the start of monitoring (in comparison with 22-week animals), but it remained unchanged during the following months. The changes in average daytime and nighttime SBP and DBP were similar. Thus, taking into account mean 24-h, daytime, and nighttime BP we can conclude that the period of our experiment corresponded to the stage of stable hypertension.

Circadian indexes calculated using SBP and DBP are presented in Table 2. The circadian index of SBP in SHR rats was higher than in the control group over the first 3 months of monitoring. This parameter was highly stable. Thus, the difference between daytime and nighttime SBP in spontaneously hypertensive rats is greater than in normotensive animals over a long period. However, this parameter approximated the control value by the end of month 4. Only in 22- and 34-week SHR rats, the circadian index of DBP was significantly higher than in control animals. At other terms of the experiment, this parameter tended to increase (in comparison with the control). Therefore, index of DBP during primary hypertension is less stable than index of SBP.

The following results were obtained during recording of 24-h SBP_{max} and SBP_{min} in SHR rats (Fig. 1). SBP_{max} significantly surpassed the initial level 1 month after the start of monitoring (by 6.74%). In 2 and 3 months, SBP_{max} did not significantly change in comparison with month 1, and at the end of month 4 this parameter slightly decreased and was not significantly higher than the initial level. SBP_{min} did not significantly differ at all experimental periods in comparison with the initial level measured in 22-week rats. The difference between SBP_{max} and SBP_{min} (Fig. 2) significantly increased by the end of month 2, in 3 months it was greater than in 2 months, but returned to the initial value by the end of month 4. The obtained data suggest that the difference between SBP_{max} and SBP_{min} increased only due to SBP_{max} rise.

TABLE 1. BP (mm Hg) in the Control (Normotensive Wistar Rats) and at Various Terms of Arterial Hypertension in SHR Rats (*M±m*)

Parameter		Control	SHR rats				
			22 weeks	26 weeks	30 weeks	34 weeks	38 weeks
Mean 24-h	SBP	117.7±4.1	189.9±4.1*	201.3±3.2*	200.2±3.7*	195.7±4.5*	201.0±4.5*
	DBP	88.1±3.8	136.2±6.2*	146.6±2.2*	142.9±3.0*	138.8±2.5*	144.9±4.4*
Average daytime	SBP	117.5±4.3	183.7±3.7*	195.8±3.5*	194.7±3.2*	189.5±4.5*	196.9±4.1*
	DBP	87.7±3.4	131.1±6.1*	143.1±2.2*	138.7±2.7*	133.6±2.5*	142.4±3.8*
Average nighttime	SBP	117.9±4.2	196.1±4.5*	206.7±2.9*	205.7±4.6*	201.8±4.3*	205.0±4.8*
	DBP	88.3±4.0	141.1±6.2*	150.1±2.2*	147.2±3.7*	144.0±2.7*	147.3±5.0*

Note. Here and in Table 2: *$p \leq 0.05$ in comparison with the control.

TABLE 2. Circadian Rhythms in the Control (Normotensive Wistar Rats) and at Various Terms of Arterial Hypertension in SHR Rats (*M±m*)

Parameter	Control	SHR rats				
		22 weeks	26 weeks	30 weeks	34 weeks	38 weeks
Index of SBP	1.01±0.02	1.07±0.01*	1.06±0.01*	1.06±0.01*	1.06±0.01*	1.04±0.00
Index of DBP	1.01±0.02	1.08±0.00*	1.05±0.01	1.06±0.02	1.08±0.01*	1.04±0.01

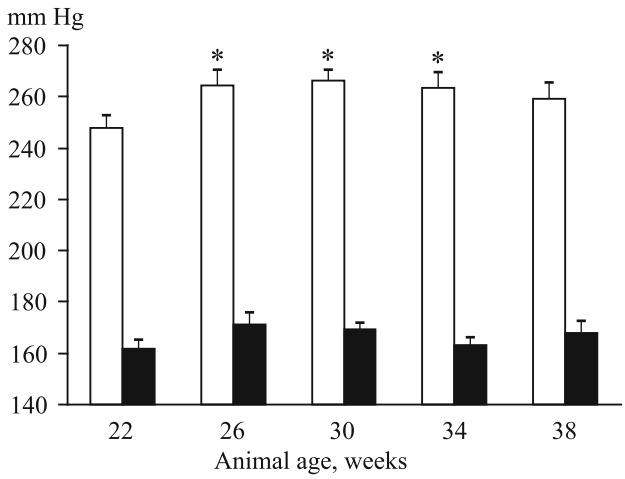

Fig. 1. 24-h SBP_{max} (light bars) and SBP_{min} (dark bars) in SHR rats at various terms of arterial hypertension. Here and in Fig. 2: *$p \leq 0.05$ in comparison with the control.

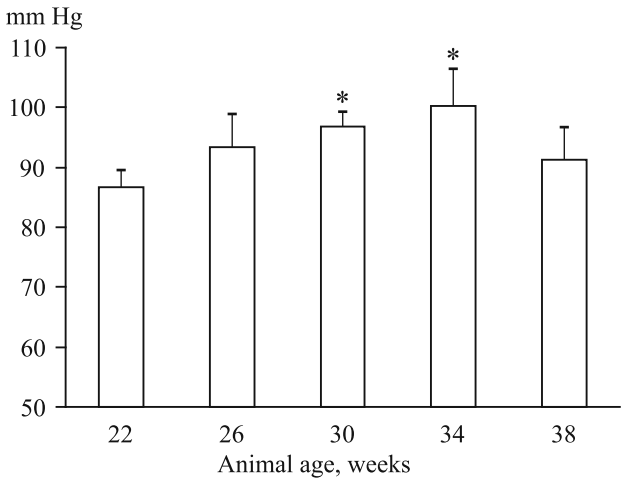

Fig. 2. Difference between 24-h SBP_{max} (light bars) and SBP_{min} (dark bars) in SHR rats at various terms of arterial hypertension.

Therefore, stably increased BP in non-treated arterial hypertension with time becomes associated with prognostically negative changes in the circadian rhythm of the main parameters of systemic hemodynamics.

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