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Circahoralian Rhythms in Assessment of Heart Rate Variability

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Circahoralian oscillations of various indices describing variations of interpulse, respiratory, and *R-R* intervals were recorded in normal subjects, in hypertensive patients, and in patients rehabilitating after cardiac infarction. The parameters of these rhythms reflect changes in the status of autonomic nervous system, correlate with pathological disturbances in circadian rhythm, and accompany the sleep-wake and wake-sleep transitions. In assessment of circadian rhythm parameters, the most informative are the plots of changes in Pierson correlation coefficients of interpulse and *R-R* intervals. The 5-min ECG segments recorded at various phases of circahoralian rhythm are subjected to circahoralian variations and can distort diagnostics.

Key Words: *biorhythms; ECG; Holter cardiac monitoring; heart rate variability; chronodiagnostics*

Circahoralian rhythms (CHR) were studied in details with recording the dozens of cell parameters [1,3]. They differ from circadian rhythm and its variations by high adaptivity and wide variations of the period ranging from 20 to 120 min [8]. CHR are often referred to ultradian rhythms resulting from disturbances of circadian rhythm [6]. However, the ultradian rhythm with the period ranging from 3 to 12 h and infradian rhythm with the period of more than 24 h indicate pathology and dramatic changes in human functional state [7]. The rhythms with a period of 12–24 h manifested themselves during the phase shifts in the circadian rhythm, although phase shift results from synchronization of CHR [4]. CHR are recorded not only in patients, but also in healthy persons and animals. Under normal conditions, they are observed not only at the cellular level, but also in tissues, organs, and functional systems of the living organism. CHR correlates with adrenal activity, cerebral electrical activity, urination, electroretinogram, vegetative (autonomic nervous system) status, digestive tract, *etc*. [10].

Our aim was to test the hypothesis on the need to take into consideration CHR during cardiac Holter monitoring in order to improve diagnostic reliability.

MATERIALS AND METHODS

To obtain 24-h records of ECG and *R-R*-intervals, we used portable cardiomonitors Valenta (Scientific-and-Production Firm NEO) and Cardio Tens (Meditex). Recording of interpulse and respiratory intervals into PC was made with original software "Family Doctor and Teacher". The software for chronodiagnostics and analysis of interpulse and *R-R* intervals was developed by Dr. Yu. V. Gurov. In addition to routine indices of heart rate variability (HRV) calculated by Holter cardiac monitoring soft-

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ware, we analyzed the dynamics of fractal dimension, Herst index, Fisher index, Baevsky index, entropy, redundancy, Pearson correlation coefficient, information dimension, correlation dimension, Rennie dimension, scaling-spectrum, chaos plot, angular dispersion and histogram, Fourier transform, and wavelet analysis data obtained with continuous and discrete transform. The raw data were recorded during sanatorium rehabilitation stage from postinfarction (n=50) and arterial hypertension (n=20) patients at the age of 50-70 years. The 24-h recorda were obtained in Rostovsky sanatorium, First Department of Internal Diseases (Rostov State Medical University), and Regional Hospital (Rostov-on-Don). The control data with interpulse and *R-R* intervals were recorded from healthy age-matched persons.

RESULTS

Analysis of daily records of *R-R* ECG intervals is usually based on averaging various indices during nocturnal and daytime within the determined hours. To reveal CHR, the sampling time should not surpass 5 min. With greater sampling periods CHR are not detected or are considered as ultradian and neglected. However, changes in autonomic status assessed by HRV indices can be revealed not only by comparing daytime and nighttime parameters, but also between various sleep phases, which alternate in parallel with CHR [2,11]. During sleep, the low-to-high frequency ratio (LF/HF) drops in comparison with the wakeful period, and elevation of this ratio indicates transition to REM stage of sleep [2]. We observed rapid oscillations with circahoralian periodicity in LF/HF not only during night, but also during daytime. To reveal these oscillations, we replaced routine physical time interval with biological time standard by putting the number of interpulse intervals along the x-axis on the plots. To compare various parameters with Baevsky index, we used averaging of 100 interpulse intervals with one-interval shift. Averaging on greater intervals (600, 4000, and 10,000) revealed the slower oscillations, which accompany CHR. The existence of rhythm hierarchy in the interpulse intervals was

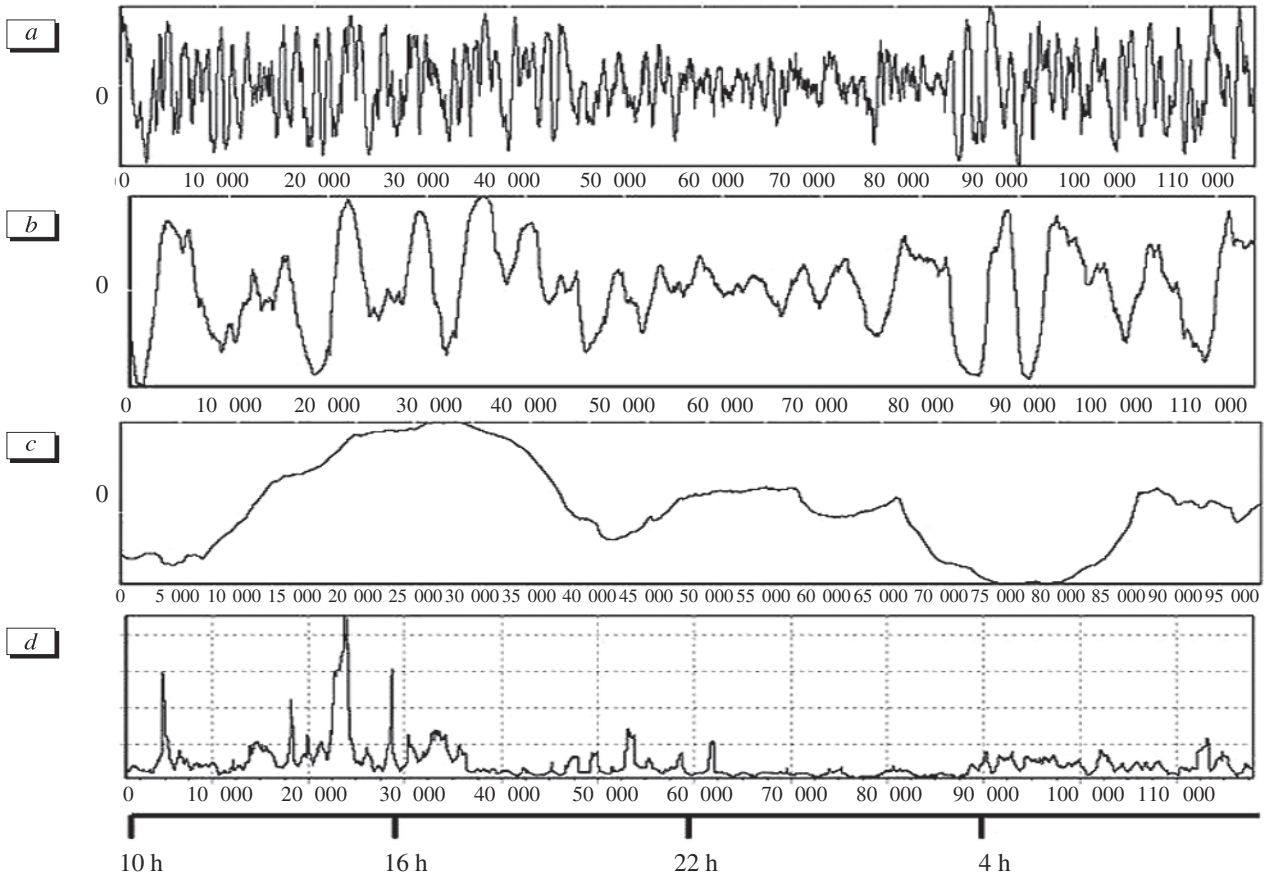

Fig. 1. The plots of Pearson correlation coefficient of *R-R* intervals obtained in 24-h ECG monitoring in patient B. demonstrating improvement of his state. Here and in Fig. 2: averaging *R-R* intervals were 100 (*a*), 600 (*b*), and 10,000 (*c*). *d*) Baevsky index calculated for 100 *R-R* intervals. Abscissa: the number of *R-R* intervals and time of the day.

corroborated by the analysis of the dynamics of fractal dimension, wavelet analyses, and by empiric decomposition into the modes. The most clear discrete hierarchical subordination of interpulse and *R-R* intervals could be observed in dynamics of Pearson correlation coefficient (Fig. 1, 2).

In addition to routine respiratory modulation and ultradian (3-12 h) and circadian (22-25) rhythms, the patients and healthy persons demonstrated rhythms with periodicity of 5-10 and 30-100 min. In healthy persons, the range of these rapid rhythms was narrower. In comparison to healthy controls, the post-infarction patients and patients with hypertension demonstrated pronounced changes in CHR parameters (predominantly, decreased amplitude and increased period and variability). In some of these patients, circadian rhythm was preserved, while in others it was virtually absent (Figs. 1, 2). In healthy persons and in most patients, CHR amplitude decreased during sleep, and the disturbances manifested themselves by the appearance of these rhythms during wake/sleep transition. The ultradian rhythms (3-12 h) were more pronounced in patients with disturbances or complete elimination of the circadian rhythm. Healthy persons had no ultradian rhythms.

CHR parameters can be used for prediction of the disease course and for evaluation of the efficiency of medication or physical therapy [5]. Here we present the plots of Pearson correlation coefficient and Baevsky index measured for *R-R* intervals in a patient, whose state improved pronouncedly in the following days according to objective evidence of instrumental and laboratory examinations (Fig. 1). Similar plot (Fig. 2) shows the data for a patient, whose state aggravated in the following days. Improvement of the state indicated by subjective assessment of the patient and by the parameters of veloergometry, blood analysis, systolic and diastolic pressure, the number and duration of the episodes of arrhythmia, extrasystole, and elevation or depression of *S-T* peak [5] correlated with smaller period and greater amplitude of CHR (Fig. 1). In contrast, unfavorable prognosis can be related to smaller amplitude of CHR accompanied by its greater variability and individuality usually coupled with disappearance or disturbance of circadian rhythm (Fig. 2).

In case of unfavorable prognosis, the mean value and deviations of Baevsky index increased (Fig. 2). In this case, elevation of the sympathetic

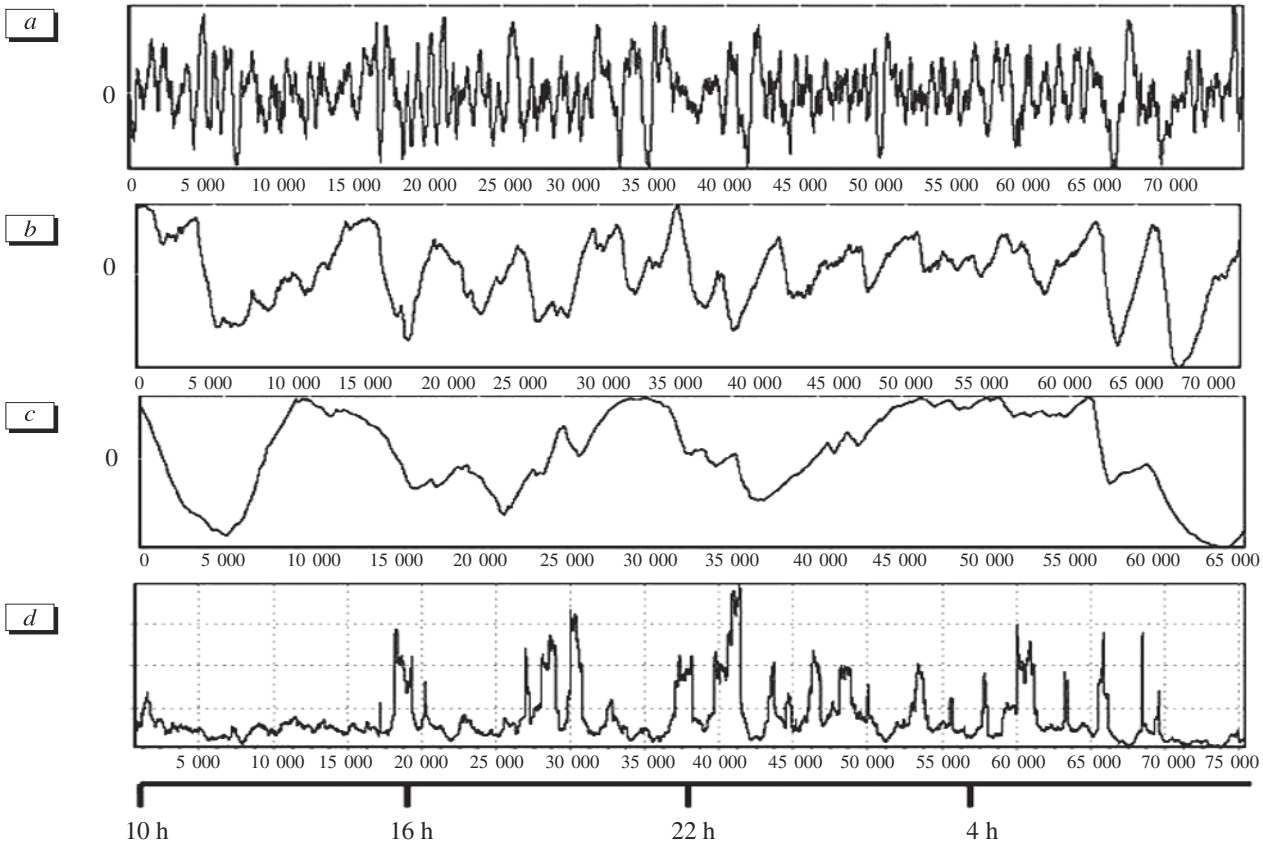

Fig. 2. The plots of Pearson correlation coefficient of *R-R* intervals obtained in 24-h ECG monitoring in patient Kh. demonstrating aggravation of his state.

tone was indicated by scatter plot, LF/HF values, dispersion, and frequency spectrum. However, similar changes were also observed in patients, whose state did not aggravate. Comparison of the plot of the changes of entropy and redundancy in these patients and in those with following aggravation of their state suggests that the changes in dynamics of Baevsky index, entropy, and redundancy indicate stress of regulatory systems of the organism. It can result in preservation of the homeostatic parameters within the normal oscillatory range or leaving this range, if the self-control in the oxygen transport system cannot be achieved only by the changes of interpulse and respiratory intervals. Increase in the mean value and deviations of Baevsky index and redundancy accompanied by decrease in the mean level and increase in entropy oscillation of interpulse and respiratory intervals can by the early markers of aggravation of patient state. In these cases, it is reasonable to limit physical load and apply preventive therapy before the onset of unfavorable changes. Simultaneous recording of interpulse and respiratory intervals as well as their ratio made with the help of various versions of original software "Family Doctor and Teacher" could differentiate the primary disturbances in cardiovascular and respiratory systems. Respiratory CHR does not simply reflect the pulse rhythm, because their period and amplitude are usually smaller. Probably, they were overlooked by this reason. For example, they are evidently present in [9] with the period of 25-30 min and can be revealed even with autoregression method according to maximum of power spectrum in a 30-sec running window.

During routine 5-min ECG recordings, it is necessary to take into account the phases of CHR in *R-R* intervals. The successive 5-min ECG records sampled for 4.5 h to plot the changes in the routine diagnostic indices at the time step of 5 min do reveal CHR. Comparison of histograms of phase pattern angles, the outline of these patterns, the scattering diagrams, and LF/HF ratio at the minimum and maximum of the corresponding CHR yields the diagnostic indices that can be contradictory. Examination carried out unintentionally during maximum or minimum of CHR can result in erroneous therapeutic strategy. This is the most important for circahoralian oscillation of autonomic balance. Such a mistake can be avoided by recording the interpulse and *R-R* intervals not for minutes, but for hours.

Thus, recording and analysis of CHR for interpulse and *R-R* intervals in ECG improve diagnosis and prognostication for the patients. Moreover, they make it possible to individually optimize the therapeutic and preventive procedures. The autonomic status and some other indices of patients or healthy persons cannot be reliably tested exclusively by 5-min records neglecting the phases of circahoralian variations.

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