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ORIGINAL ARTICLE

Correlative Connections between Chronostructures of Water-Mineral Homeostasis and Weather Indices in Cardiovascular Pathology

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Objective: In this article, we studied the chronoperiodical system of homeostasis of electrolytes and trace elements and their correlative connections with the rhythms of hydrometeorological indices in cardiovascular pathology and in healthy individuals. **Methods:** Two hundred patients with cardiovascular pathology and 70 healthy subjects were on unified regimen. Urine was collected with 4-h portions, during 72–120 h (3–5 days). Each specimen was analyzed for macro- (sodium, potassium, calcium, magnesium, chlorine, phosphorus) and microelements (ferrum, cuprum, zinc, chromium, cadmium, vanadium). Rhythms parameters have been estimated by nonlinear least squares method for sinusoidal rhythms and dispersion analysis for nonsinusoidal rhythms. Data of weather indices were received from the Hydrometeorological Service of Armenia. **Results:** In the healthy subjects, statistically significant rhythms were observed in 91% of rhythmological investigations of urinary excretion electrolytes and trace elements. Acrophases of rhythms were mostly individual. On the early stage of hypertension and ischemic heart disease, electrolytes and trace elements rhythms were statistically nonsignificant in 22–23% of cases. Among significant rhythms, the infradians prevailed (46–53%). In the late stage of hypertension and ischemic heart disease, the rhythms of electrolytes and trace elements were statistically nonsignificant in 31–32% of cases. In patients with cardiovascular pathology, statistically significant correlative connections between rhythms of water-mineral homeostasis and rhythms of weather indices differ in comparison with the results of practically healthy individuals. **Conclusion:** Examination results of patients with cardiovascular pathology showed a direct influence of hydrometeorological indices on a temporal structure of an organism as well as a decrease of adaptive possibilities of homeostasis of electrolytes and trace elements.

Key Words: Biorhythm; Mesor; Amplitude; Acrophase; Electrolyte; Trace element

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INTRODUCTION

Chronoperiodical systems and dynamics of biological rhythms evolved in the process of evolution under the influence of environmental factors [1-4]. Circadian structure had been considered as a fundamental rhythm of biological objects. With the discovery of the solar wind, the magnetic field, Earth's magnetosphere it became obvious that the biorhythms and magnetic factors have similar rhythms [1]. The role of macro- and microelements in human nutrition as well as their function in health and disease were

extensively reviewed [5-9]. Convincing data about macro- and microelements metabolism disturbance in patients with hypertensive disease and ischemic heart disease (IHD) on different stages of its development are obtained by different authors [5,10,11]. Nevertheless, the results of these investigations are contradictory. It partly was due to absence of unification of methods, conditions of investigation, patients' grouping and normal values. Besides, these investigations were mostly carried out without taking into account the chronostructure of an organism [5,10]. In the given paper, we studied the rhythms of electrolytes and trace elements homeostasis and their correlative connections with the fluctuations of hydrometeorological indices in patients with cardiovascular pathology and in healthy individuals.

METHODS

Participants and data collection

Seventy practically healthy subjects (25 females and 45 males) and 100 patients with hypertension (H) and 100 with IHD were investigated. Fifty patients with H were on the first stage (H1) and 50 patients with H were on II, II–III stages (H2). Clinical classification of hypertension and blood pressure were conducted according to Global Hypertension Practice Guidelines which was suggested by International Society of Hypertension [12]. One hundred males with IHD (stable stenocardia) were investigated [42 males with functional class II (IHD1) and 58 males with functional class II–III, III (IHD2)]. Twenty-four patients with IHD had a myocardial infarction in the past. Those patients were investigated no earlier than 6 months after acute myocardial infarction. Functional classification was conducted according to classification which was suggested by Canadian Cardiovascular Society [13]. Control group consisted of healthy individuals whose clinical and laboratory investigations were within normal limits. The average age of healthy subjects was 49.2±2.0 years and that of patients was 54.2±3.0 years. The healthy subjects and patients were on unified regimen of diet, sleep and wakefulness (from 07:30 until 22:30). Urine was collected with 4-h portions during 72–120 h (3–5 days) in the healthy subjects and patients. Total Na, K, Ca, Mg, Fe, Cu, Zn, Cr, Cd, V were analyzed on the Perkin-Elmer (USA) atomic absorption spectrophotometer (AAS). P was analyzed with "Phosphorus" kits (Viola LLS, Yerevan, Armenia), Cl was analyzed on Cobas b 121 system (Germany). The data of hydrometeorological indices (HMI) were received at 3-h intervals from the Hydrometeorological Service of Republic of Armenia.

- The temperature of the air (TA, °C)
- The relative humidity of the air (RHA, %)
- The deficit humidity of the air (DHA, hPa)
- The atmospheric pressure (AP, hPa)
- The speed of wind (SW, m/s)
- The general cloudiness (GC, mark)

Rhythmological analyses of TA, RHA, DHA, AP, SW, and GC were conducted for the disclosure of ultradian, circadian, and infradian rhythms during 7–10 days.

All procedures were performed in accordance with the ethical standards of the research committee and were implemented in accordance with the World Medical Association's Declaration of Helsinki.

Statistical analysis

For the estimation of the period of the rhythm, we used two methods: 1) an approximation method and a 2) method of estimating the repetition of the following one after other fragments of the investigated process. By means of the approximation method, sinusoidal rhythms with known (cosinor) [14] and unknown periods (nonlinear least-squares) [15,16] are revealed. When analyzing sinusoidal rhythms, the following mathematical model was used in both the single cosinor [14] and the nonlinear least squares method: $Y(t)=g(t)+x(t)$, where $g(t)=M+A\cos(w(t)+\varphi)$ and x(t) was the normally distributed white noise. In contrast to the approach in single cosinor where only the mesor (M), amplitude (A), and the acrophases (φ) were unknown, in the nonlinear least squares $W=2\pi/T$ (T was the period of rhythm) was also an unknown parameter. In such an approach, the ordinary procedures of least squares were not suitable and the problem was solved by means of combination of the method of successive approximation. In that case when with the nonlinear least squares statistically significant rhythms were not revealed, we used the method estimating the repetition of the following one after other fragments of the process which was based on the method of dispersion analysis [16]. According to one-dimension dispersion analysis t (the components of dispersion) and the F-ratio were computed. The duration of the fragment checked for repetition the calculated F of which was greater than the table F determined the period of rhythms. Analyzing the results, we grouped the rhythms according to the range of periods suggested by the International Society for Chronobiology [17-19] with some modifications proposed by Aslanian et al. [20]. The rhythms with a period ranging from 3 h to 20 h were considered to be ultradian, from 20 h to 28 h circadian, and from 28 h to 96 infradian.

RESULTS

The results showed that in healthy subjects 91% of macro- and microelements excretion rhythms were statistically significant. Among the significant rhythms of macro- and microelements excretion the circadian prevailed (92%). The results showed that in the healthy subjects 3.8% of macro- and microelements excretion rhythms were nonsinusoidal. Thus, healthy subjects were characterized with the circadian rhythms and definite value of mesors and amplitudes. Acrophases of the rhythms were mostly individual. Our data witnessed that in the early stages of H (H1) and IHD (IHD1) the macro- and microelements excretion rhythms in 22–23% were statistically nonsignificant. Among the significant rhythms of electrolytes and trace elements excretion infradian

prevailed (46–53%). Mesors of sodium, phosphorus, cuprum, zinc, chromium, cadmium (H1) and phosphorus, ferrum, cuprum, zinc, chromium and vanadium (IHD1) excretion rhythms were statistically significantly higher than in the healthy subjects. The results showed that in early stages of H (H1) amplitudes of coefficient Na/K, P, Zn, Cd and Cl, P, Fe, Cu, Zn of IHD (IHD1) were significantly higher than in the healthy subjects. Mesors of Mg (H1), Ca, Mg (IHD1) and amplitudes of coefficient Na/K, Ca, Mg (H1) and coefficient Na/K, Mg (IHD1) were significantly lower than in the healthy subjects. Statistically significant rhythms of macro- and microelements excretions were not revealed in most of the patients in the late-stage H (H2, 32%) and IHD (IHD2, 31%). However, among statistically significant rhythms the circadians prevailed (48–54%). Mesors of K, P, Zn, Cr, Cd, V (H2), Cl, P, Zn, Cr, V (IHD2) and amplitudes of P, Zn (H2), Cl, P, Zn (IHD2) excretion rhythms were significantly higher than in the healthy subjects. Mesors of Mg (H2), Ca, Mg (IHD2) and the amplitudes of volume of urine, coefficient Na/K, Ca, Mg (H2), coefficient Na/K, Ca, Mg (IHD2) were significantly lower than in the healthy subjects.

For realization of correlative investigation, we measured macro- and microelements in urine. Measurements were done within 3–5 days, at 3-h intervals. After we used sliding method with the same 3–5 days, previous and following 2-days at 3-h intervals measuring of HMI. Investigations were carried out by Spirmen's

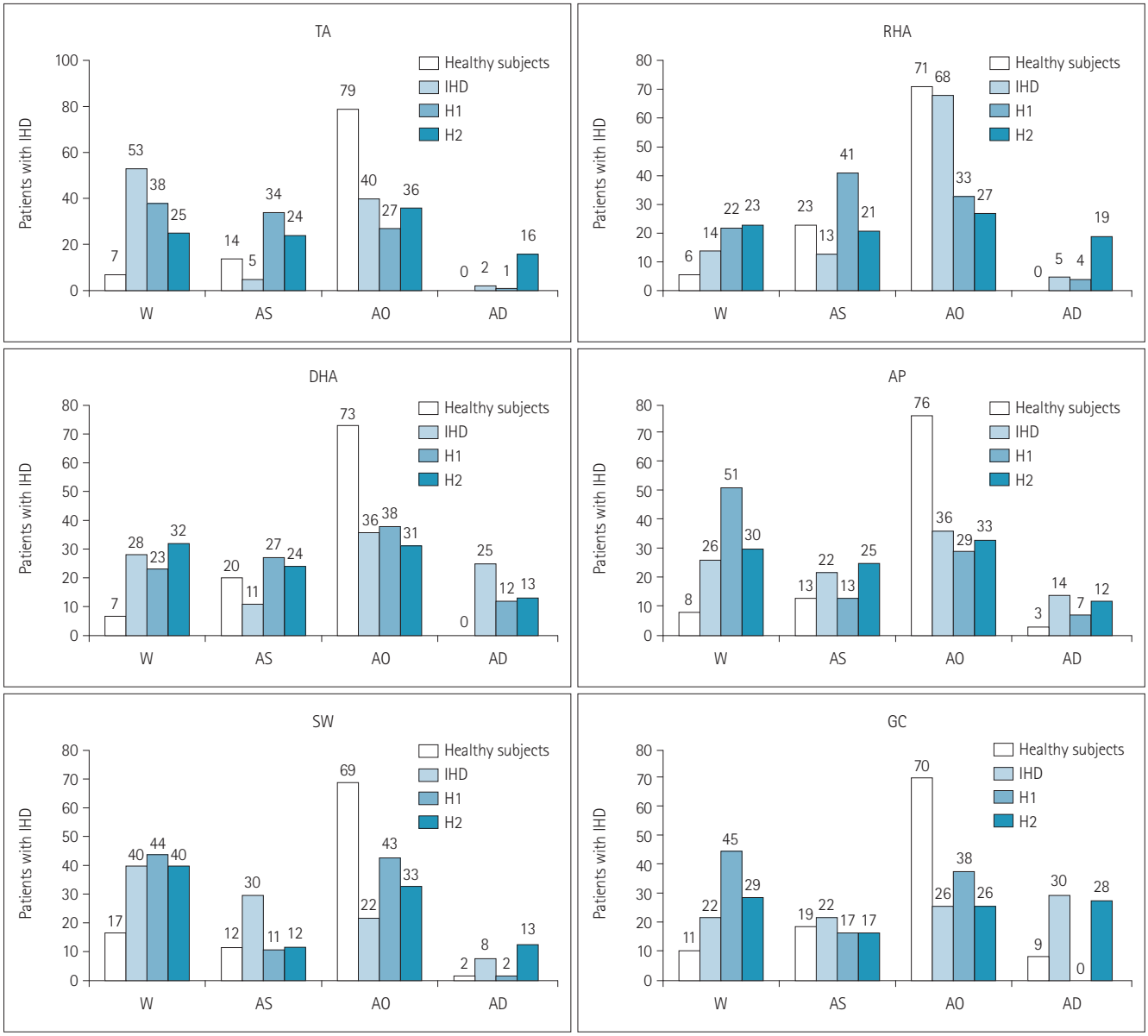

Figure 1. Summary data of the acrophases of excretion rhythms of electrolytes and trace elements relative to the acrophases of HMI rhythms (TA, RHA, DHA, AP, SW, GC) in healthy subject and patients. W: number (%) of healthy subjects and patients with statistically nonsignificant correlative connections between rhythms of water-mineral homeostasis and HMI rhythms. AS: number (%) of healthy subjects and patients with acrophases of water-mineral excretion rhythms which occurred simultaneously with the acrophases of the HMI rhythms. AO: number (%) of healthy subjects and patients with outstripped acrophases of water-mineral excretion rhythms relative to acrophases of the HMI rhythms. AD: number (%) of healthy subjects and patients with delayed acrophases of water-mineral excretion rhythms relative to acrophases of the HMI rhythms. IHD: ischemic heart disease, HMI hydrometeorological indices, TA: temperature of the air, RHA: relative humidity of the air, DHA: deficit humidity of the air, AP: atmospheric pressure, SW: speed of wind, GC: general cloudiness.

method with sliding data of each mineral with the data of each HMI at 3-h intervals. The presence of correlative connections between curves was considered statistically significant with coefficient of correlation 0.5 and more. Since the data of HMI were registered at 3-h intervals, 4-h data of urine and minerals were corrected with the plan of interpolation. Our data indicated that healthy subject's excretion rhythms of water-mineral homeostasis had significant correlative connections (91%) with the rhythms of HMI (external synchronization). Correlative conjunctions of indices were investigated taking into account the outstrip or delay of the acrophases of biorhythms relative to the acrophases of the HMI rhythms. Our data indicated that in healthy subjects the acrophases of the rhythms of homeostasis of water-mineral indices were outstripped (73%) to the acrophases of rhythms HMI. In healthy subjects, the acrophases of the rhythms of excretion of electrolytes and trace elements in 15% of cases occurred simultaneously with acrophases of HMI rhythms (Figure 1). The results of patients with H1 have shown a 37% statistically nonsignificant correlative connections between their water-mineral homeostasis and the rhythms of HMI. In patients with H, correlative connections between rhythms of Fe, Cd (H1), Zn, Cr (H2) and TA; Na, K, Cd, V (H1), Cu, Zn, Cr (H2) and RHA; Ca, Fe, Cd, V (H1) and DHA; Cd (H1, H2), Cu, Zn, Cr (H2) and AP; Zn (H1), Cd (H2) and SW; Zn, Cd (H1) and GC were statistically significant. Our results indicated that in patients with H, acrophases of the rhythms of water-mineral excretion outstripped 35% (H1) and 32% (H2) to the acrophases of the HMI rhythms (Figure 1). These data obviously were statistically significantly smaller in comparison with results of the healthy subjects ($p<0.001$). Patients with IHD1 and IHD2 were combined into one group because the results of their correlation investigations were similar. Our results indicated that in individuals with IHD acrophases of electrolytes and trace elements homeostasis outstripped (38%) to the acrophases of the HMI rhythms (Figure 1). These data were statistically significantly smaller in comparison with the results of the healthy subjects ($p<0.001$). Our results indicated that individuals with IHD acrophases of water-mineral homeostasis in 17% of cases were simultaneous with the acrophases of rhythms HMI (Figure 1). In patients with IHD, correlative connections between rhythms of Cd and TA; Cl, P, Cr, Cd, V and RHA; Cd, Cu, Cr and DHA; Fe, Cr, V and AP; Cd and SW; Fe, Cr, Cd, V and GC were statistically significant.

DISCUSSION

Our results showed that in healthy subjects chronostructure of the water-mineral homeostasis was sinusoidal and circadian. It was stated to be an internal synchronization by period of rhythms. We were unable to compare our data with the results of other authors since similar investigations in healthy subjects and in patients with cardiovascular pathology have not been found in available literature.

Circadian fluctuations in urinary excretion of electrolytes and trace elements have been reported by Kanabrocki et al. [9]. These authors investigated circadian changes by observing each subject for 27 h and using cosinor analysis. By that approach, one can answer only the question whether or not there was a circadian sinusoidal fluctuation. Our data of electrolytes (Na, K, Ca, Mg, P) and trace elements (Fe, Cu, Zn, Cr, Cd) excretion rhythms were different from the results reported by Kanabrocki et al. [9]. These differences were connected with ecological, biogeochemical peculiarities and the difference of biorhythmological approach. Our data indicated that there were macro- and microelements excretion rhythms changes in the patients with cardiovascular pathology beginning from the early stages (H1, IHD1), which were expressed in the alterations of the parameters of fluctuations in comparison to the data of the healthy individuals. The synchronization by fluctuation period was inherent for normal functions of the organism. Thus, the new neuroendocrine status of the organism reorganized the circadian chronostructure of water-mineral internal system for preservation of relative stationary of the macro- and microelements compositions in the internal environment at the early stages of cardiovascular pathology. Those protective reactions went out slowly in the late stages of H and IHD (H2, IHD2). The results also showed that in the patients with H and IHD depending to the gravity of the pathological state, in 31–32% statistically significant rhythms of macro- and microelements excretion were not revealed. Thus, the changes of parameters of the macro- and microelements excretion rhythms in urine obtained early diagnostic significance. Those data could also help in the organization of pathogenetic therapy in patients with cardiovascular pathology taking into account the chronostructure of water-mineral homeostasis. Our results showed that healthy subjects' excretion rhythms of macro- and microelements had significant correlative connections with the rhythms of HMI (external synchronization). The data of patients with H1 and IHD1 have shown 31–37% statistically nonsignificant correlative connections between biorhythms and the rhythms of HMI (external desynchronization). In patients with H, acrophases of biorhythms often were simultaneous [21–24% (H1, H2) and 17% (IHD)] or delayed [14–17% (H2, IHD)] relative to the HMI rhythms (Figure 1). That data indicated the direct influence on the chronoperiodical system of an organism by the fluctuations of HMI and decrease of adaptive possibilities of water-mineral homeostasis in patients with cardiovascular pathology. Thus, practically healthy subjects were characterized with circadian organization of water-mineral homeostasis and with synchronization by period of rhythms. In healthy individuals, acrophases of macro- and microelements homeostasis outstripped the acrophases of the rhythm of HMI. Chronostructure of water-mineral homeostasis in patients with early stage of IHD and H characterized with infradian organization. In cardiovascular disease, acrophases of biorhythms often were concurrent or delayed relative to the acrophases of the rhythms of HMI.

In this article, some data of our last investigations were summarized [7,8,21] and characterized the nuances of internal and external synchronization or desynchronization.

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Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Author Contributions

Conceptualization: Lyusya A. Babayan, Hamlet G. Hayrapetyan. Data curation: Lyusya A. Babayan. Formal analysis: Anahit E. Meliksetyan, Tsoghik G. Harutyunyan. Funding acquisition: Hrachya A. Vardanyan. Investigation: Ara K. Gulyan, Pargev K. Sarafyan, Hrachya A. Vardanyan, Zarmandukht S. Petrosyan, Lianna M. Pogosyan. Methodology: Hayk E. Danoyan, Lyusya A. Babayan. Project administration: Hrachya A. Vardanyan. Resources: Hrachya A. Vardanyan. Software: Eduard H. Danoyan. Supervision: Lyusya A. Babayan. Validation: Lyusya A. Babayan. Visualization: Hrachya A. Vardanyan. Writing—original draft: Hrachya A. Vardanyan. Writing—review & editing: Hrachya A. Vardanyan.

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