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Temporal Organization of Electrolytes and Trace Elements Homeostasis in Cardiovascular Pathology and in Immobilization Stress

Babayan LA[1], Chibisov SM[2], Gulyan AK[3], Sarafyan PK[3], Ivanyan SA[4*], Mirzoyan IA[4], Gasparyan NA[4], Paronikyan RG[5], Gaboyan GS[6] and Zohrabyan MA[6]

1 Chair of Pathological Physiology, Department of Medicine, Armenian Medical Institute, Yerevan, Armenia
2 Peoples Friendship University of Russia, Chair of Pathophysiology of V.A. Frolov, Moscow, Russia
3 Erebuni Medical Center, Department of Urgent Cardiology, Yerevan, Armenia
4 Chair of Pathological Physiology, Armenian Medical Institute, Yerevan, Armenia
5 Chair of Pharmacology, Department of of Biology, Armenian Medical Institute, Yerevan, Armenia
6 Chair of Therapy, Armenian Medical Institute, Yerevan, Armenia

***Corresponding author:** Dr. Susi Ivanyan

Susanna.ivanyan@yandex.ru

Lecturer, Chair Pathological Physiology, Armenian Medical Institute, Yerevan, Armenia.

Tel: + 037495137569

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Abstract

Four hours urine and blood specimen were collected over a span of 48-120 hours from 70 healthy subjects, 100 patients with ischemic heart disease, 100 hypertensive patients, 15 intact rabbits, 20 rabbits under the action of stress. Each specimen was analyzed for electrolytes (Na, K, P, Cl, Ca, Mg) and trace elements (Fe, Cu, Zn, Cr, Cd, V). Rhythm parameters were estimated by dispersion analysis for non-sinusoidal rhythms and by nonlinear least squares method for sinusoidal rhythms. In the healthy subjects in 91% cases of rhythmological investigations urinary excretion electrolytes and trace elements statistically significant rhythms were observed. In the healthy subjects and in the intact rabbits the rhythms of electrolytes and trace elements were circadian in 75-92% of cases. Acrophases of rhythms were mostly individual. In early stage of cardiovascular pathology and in the rabbits under the action of stress the rhythms of electrolytes and trace elements were statistically non- significant in 20-43% of cases. Among significant rhythms the infradian ones (45-60%) prevailed. In late stage of cardiovascular pathology the rhythms of electrolytes and trace elements were statistically non-significant in 31-33% of cases. Among the significant rhythms the circadian ones (48-54%) prevailed.

Keywords: Cardiovascular pathology; Chronobiology; Corticosterone

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Introduction

The role of electrolytes and trace elements in human nutrition as well as their function in health and disease were extensively reviewed [1-7]. Convincing data about metallic elements metabolism disturbance in patients with atherosclerotic and hypertensive diseases on different stages of its development are obtained by different authors. Nevertheless, the results of these investigations are contradictory. It was connected partly with the 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 temporal structure of the organism. Chronobiology was rightly recognized as an essential adjunct to the study of man. The significance of electrolytes and trace elements in human metabolism should be investigated more clearly from the stand point of time structure. Temporal discordance was the early stage of development of the majority of pathological changes and diseases [8]. In the given paper the rhythms of electrolytes and trace elements homeostasis in cardiovascular pathology and healthy subjects studied.

Patients and Methods

70 practically healthy subjects (25 female and 45 male), 100 male with ischemic heart disease [(IHD) (40 male with functional class II, II-III (IHD I) and 60 male with functional class III, IV (IHD2)], 100 hypertensive patients (40 female and 60 male). 50 patients with hypertension were 1 stage (H1) and 50 patients with hypertension were II, III stages (H2) were investigated. 26 of patients with IHD2 had had myocardial infarction before and had been investigated not earlies than 6 months after acute myocardial infarction. The average age of the healthy subjects was 49.2 ± 2.0 years and that of patient's 54.2 ± 3.0 years. The healthy subjects and patients were in united regimen of diet, sleep and wakefulness (from 07.30 till 22.30). Urine was collected with four hour portions 72-120 h (3-5 days) in the healthy subjects and patients.

The rabbits were used in the experimental work. The first series of the experiments was made on the intact animals (15 rabbits). 20 rabbits were used in the second series of the experiments. The rabbits were subjected to stress daily 1.0-1.5 hours immobilization and to the effects of electric stimulation. The experiment lasted 2 weeks.

Four-hour urine and blood specimens were collected over a Spain 48-72 hours (on the second series these procedures started to be followed on the 12th day of the experimental work). An assessment of action of hypothalamo – hypophysical suprarenal system was made on the basis the growth of mesor and amplitude of rhythms of the blood corticosterone. The quantitative determination of the corticosterone contained in the plasma was based on radioimmunological analysis (kits PUH –B- 3H, RF).

Total Na, K, Cu, Mg, Fe, Ca, Zn, Cr, Cd were determinate on Perkin – Elmer (USA) atomic absorption spectrophotometers (AAS). P was determinate with "Phosphorus" kits (Viola LLS, Armenia), Cl was determinate on Cobas b 121 system (Germany) [9-11].

The rhythm parameters were estimated by dispersion analysis for non-sinusoidal rhythms and by nonlinear least squares method for sinusoidal rhythms [12]. The rhythms were grouped in accordance with the glossary of chronobiology which was subjected to some changes. The rhythms with a period ranging from 3 to 20 hours were considered to be ultradian, from 20 to 28 hours – circadian and from 28 to 96 hours- infradian [6,7].

The results showed that in the healthy subject 91% of electrolytes and trace elements excretion rhythms were statistically significant. Among the significant rhythms of electrolytes and trace elements excretion the circadian 92% prevailed. In the cases when the healthy subject's significant sinusoidal rhythms were not observed non-sinusoidal rhythms were obtained by the program of dispersion analysis. The results showed that in the healthy subjects 3.8% of electrolytes and trace elements excretion rhythms were non-sinusoidal. Circadian variation in the urinary excretion of electrolytes and trace elements had been reported by Kanabrocki et al. [11]. These authors had investigated circadian changes by observing each subject 27 h and using cosinor analysis. By that approach one could answer, only the question was if there was a circadian sinusoidal fluctuation.

Nevertheless, our data of excretion rhythms of electrolytes and trace elements concerning other parameters (mesor and amplitude) of rhythm, besides the period in the healthy subjects were almost similar to the reported by Kanabrocki et al. [11]. Mesors and amplitudes were different from the data reported by Kanabrocki et al. which were connected with the ecological and biogeochemical peculiarities.

Thus healthy subjects were characterized with the circadian rhythms and with definite value of mesor and amplitude within the confidence limit. But the acrophases of rhythms were mostly individual and not definite for the total group of the healthy subjects.

Our data witnessed that in the early stage of IHD1 the electrolytes and trace elements excretion rhythms 23% were statistically non-significant. Among the significant rhythms at electrolytes and trace elements excretion infradian prevailed (53%). Mesors of Na, Cl, P, Fe, Cu, Zn, Cr, V excretion rhythms statistically significantly higher than in the healthy subjects **(Table 1).**

The results showed that in early stage of IHD1 amplitude of coefficient Na/ K, Cl, P, Fe, Cu, Zn were significantly higher than in the healthy subjects. Mesors of Ca, Mg and the amplitudes of coefficient Na/K, Mg significantly lower than in the healthy subjects **(Table 1).** Statistically the significant rhythms of electrolytes and trace elements excretion were not revealed in most of the patients in the late stage of IHD2 (31%). But among the statistically significant rhythms the circadian (54%) prevailed **(Table 2).** In the late stage of IHD2 mesors of Cl, P, Zn, Cr, V and amplitudes of Cl, P, Zn excretion rhythms were significantly higher than in the healthy subjects **(Table 2).** In the late stage of IHD2 mesors of Ca Mg, and amplitudes of coefficient Na/k, Ca, Mg excretion rhythms were significantly lower than in the healthy subjects **(Table 2).**

Our data witnessed that in the first stage of hypertensive disease (H1) the rhythms of electrolytes and trace elements excretion were statistically non-significant (22%). Among the statistically significant rhythms the infradian (46%) prevailed. In the H1 mesors of Na, P, Cu, Zn, Cr, Cd and amplitudes of P, Zn, Cd excretion rhythms were significantly higher than in the healthy subjects **(Table 3).**

In the H1 mesor of Mg and the amplitudes of volume of the urine coefficient Na/K, Ca, Mg excretion rhythms were significantly lower than in the healthy subjects **(Table 3).** Our data witnessed that in the late stages of H2 electrolytes and trace elements excretion rhythms 32% were statistically non-significant. Among the significant rhythms the circadians prevailed (48%). In the H2 mesors of K, P, Zn, Cr, Cd, V and amplitudes of P, Zn, the excretion rhythms were significantly higher than in the healthy subjects **(Table 4).** In the H2 mesor of Mg and the amplitudes of volume of urine, coefficient Na/K, Ca, Mg were significantly lower than in the healthy subjects **(Table 4).**

Table 1 Mesors (M) and amplitudes (A) of urinary excretion of the electrolytes and trace elements and ultra – (U), circa (C) and infradian (I) distribution (%) of the statistically significant rhythms (S) in IHD 1.

Indices	S	U	C	I	Mesor ± SE	Amplitude ± SE
Volume of Urine	90	6	33	61	44.93 ± 3.67	15.84 ± 1.93
Na	70^{xxx}	7	21	72	6.37 ± 0.5*	2.37 ± 0.28
K	78^{x}	6	42	52	1.93 ± 0.13	0.69 ± 0.05
Na/K	63	9	64	27	3.41 ± 0.2	0.85 ± 0.09*
Cl	85	12	23	65	11.83 ± 1.18**	5.15 ± 0.79**
Ca	79	10	45	45	76.15 ± 12.02***	32.43 ± 5.53
Mg	56^{x}	20	20	60	44.32 ± 5.16***	16.01 ± 2.82**
P	76	23	69	8	2.19 ± 0.36**	0.98 ± 0.25*
Fe	100	50	10	40	203.21 ± 19.09**	107.61 ± 12.07***
Cu	80	0	37	63	75.12 ± 5.44**	32.08 ± 3.10***
Zn	89	0	25	75	0.38 ± 0.04**	0.22 ± 0.03***
Cr	44^{x}	0	0	100	34.30 ± 0.95**	11.32 ± 1.48
Cd	67^{x}	17	0	83	15.48 ± 0.62	5.92 ± 0.41
V	56	20	40	20	36.10 ± 4.67*	12.11 ± 21
Total Percent	77^{xxx}	11	36	53		

Note: x - < 0.05; xx $p < 0.01$; xxx $p < 0.001$ they were calculated comparably with data of the healthy subjects.
Mesors and amplitudes were calculated by the following units: volume of urine ml/hour; Na, K, P, Cl-mmol/hour; Ca, Mg, Zn – µmol/hour; Fe, Cu, Cr, Cd, V – nmol/hour here and in the others tables.

Table 2 Mesors (M) and amplitudes (A) of urinary excretion of the electrolytes and trace elements and ultra – (U), circa (C) and infradian (I) distribution (%) of the statistically significant rhythms (S) in IHD 2.

Indices	S	U	C	I	Mesor ± SE	Amplitude ± SE
Volume of Urine	78^{x}	13	68	19	41.73 ± 1.87	13.90 ± 0.95
Na	72^{x}	12	67	21	5.78 ± 0.32	2.13 ± 0.15
K	75^{xxx}	30	40	30	1.82 ± 0.12	0.65 ± 0.05
Na/K	53^{xxx}	9	38	53	3.59 ± 0.29	0.83 ± 0.08**
Cl	76^{xxx}	11	54	35	9.76 ± 0.90**	4.30 ± 0.56**
Ca	70^{xx}	24	52	24	82.46 ± 5.75**	30.46 ± 2.52**
Mg	66^{x}	17	57	26	56.11 ± 5.41^{xx}	19.48 ± 1.94**
P	68^{x}	15	58	27	2.09 ± 0.15^{xxx}	0.80 ± 0.07***
Fe	61^{xxx}	21	58	21	134.96 ± 9.45	56.55 ± 5.71
Cu	72^{x}	24	43	33	48.32 ± 5.19	20.02 ± 2.41
Zn	64^{x}	44	25	31	0.43 ± 0.05$^{xx\,x}$	0.18 ± 0.02***
Cr	63^{x}	0	92	8	33.25 ± 2.63^{x}	12.03 ± 1.46
Cd	67^{xx}	20	70	10	14.89 ± 1.67	6.35 ± 1.05
V	75	25	33	42	36.27 ± 2.59^{xx}	14.07 ± 1.73
Total Percent	69^{xxx}	18	54	28		

Our data witnessed that the patients with the cardiovascular pathology beginning from the early stages (IHD 1 and H1) electrolytes and the trace elements excretion rhythms changes took place which were expressed in the alterations of the period, mesor and amplitude in compassion with the data of the healthy subjects.

A prolonged stress-reaction was important in the uprise and progressing of the cardiovascular pathology. Obviously, reorganization of the circadian structures of the water - mineral homeostasis in IHD1 and H1 was the result of the new neuroendocrine status of organism. It supposition was undergone the experimental examination by us **(Table 5).**

Generalizing the data of the rhythmological research of the water -mineral system we came to the following conclusion: the majority of the intact rabbits had the circadian rhythms of the water-mineral homeostasis and the rhythms had a certain value of the mesors and amplitudes. The aerophase of the rhythms had an individual character. And at the same time there was a 6-12 hours difference between aerophases of the same water- mineral homeostasis in the sense in the plasma and urine Under the influence of stress factors the water- mineral system, recognized its temporal structure which was expressed in transformation of the circadian rhythms into non-periodical variations or the infradian rhythms. The rhythms of water- mineral homeostasis of blood were characterized by the changes of periods and amplitudes and the efferent components were by changes of periods, characterized mesors and amplitudes. Logically due to the lability of parameters of the water-mineral homeostasis, the constancy of the blood mesors was preserved.

Table 3 Mesors (M) and amplitudes (A) of urinary excretion of the electrolytes and trace elements and ultra – (U), circa (C) and infradian (I) distribution (%) of the statistically significant rhythms (S) in H 1.

Indices	S	U	C	I	Mesor ± SE	Amplitude ± SE
Volume of Urine	75^{x}	10	67	23	48.21 ± 1.94	10.02 ± 1.11*
Na	83^{x}	18	58	24	6.94 ± 0.41***	2.08 ± 0.17
K	93	8	46	46	2.37 ± 0.24	0.67 ± 0.08
Na/K	76	23	27	50	3.41 ± 0.30	0.76 ± 0.10**
Cl	82	0	43	57	9.08 ± 1.06	3.24 ± 0.69
Ca	92	0	42	58	93.94 ± 5.82	33.88 ± 2.50*
Mg	83	0	40	60	48.93 ± 6.06**	14.28 ± 1.53***
P	56^{xx}	10	40	50	2.17 ± 0.27***	0.65 ± 0.08*
Fe	64^{xx}	11	33	56	134.42 ± 10.16	44.46 ± 4.41
Cu	50^{xx}	14	43	43	73.28 ± 4.23*	24.10 ± 4.10
Zn	64	0	45	55	0.41 ± 0.04***	0.20 ± 0.03***
Cr	100	0	43	57	34.37 ± 4.08*	15.23 ± 1.70
Cd	100	0	33	67	22.98 ± 2.52**	6.74 ± 0.79*
V	67	0	0	100	24.71 ± 0.74	10.32 ± 2.11
Total Percent	78^{xxx}	9	45	46		

Table 4 Mesors (M) and amplitudes (A) of urinary excretion of the electrolytes and trace elements and ultra – (U), circa (C) and infradian (I) distribution (%) of the statistically significant rhythms (S) in H 2.

Indices	S	U	C	I	Mesor ± SE	Amplitude ± SE
Volume of urine	62$^{x\,xx}$	6	78	16	42.23 ± 2.14	10.35 ± 35 ± 1.07*
Na	62^{xxx}	6	51	43	6.26 ± 0.54	2.17 ± 0.22
K	73^{xx}	16	41	43	2.62 ± 0.16***	0.95 ± 0.10
Na/K	72	25	35	40	3.18 ± 0.18	0.81 ± 0.06**
Cl	64^{xx}	22	61	17	8.00 ± 0.65	2.94 ± 0.41
Ca	60^{xxx}	7	40	53	100.8 ± 6.24	28.71 ± 2.34***
Mg	77	26	44	30	38.82 ± 3.66***	11.58 ± 1.62***
P	53^{xxx}	21	42	37	2.85 ± 0.25***	1.16 ± 0.22***
Fe	83^{x}	5	84	11	147.01 ± 10.36	50.79 ± 6.41
Cu	64^{xxx}	29	14	57	44.40 ± 3.59	17.00 ± 2.81
Zn	70	29	14	57	0.49 ± 0.04***	0.26 ± 0.07**
Cr	60^{x}	16	42	42	32.94 ± 2.41*	10.03 ± 1.91
Cd	79^{x}	18	64	18	17.49 ± 0.98*	5.79 ± 0.65
V	67	50	17	33	36.58 ± 4.22*	13.58 ± 2.82
Total per cent	68^{xxx}	17	48	35		

Table 5 Mesors (M) and amplitudes (A) of urinary excretion of the electrolytes and trace elements and ultra – (U), circa (C) and infradian (I) distribution (%) of the statistically significant rhythms (S) in immobilization stress.

Indices	S	U	C	I	Mesor ± SE	Amplitude ± SE	A/M %
Volume of Urine	(3) 50	0	25	75	226.9 ± 7.7	200.0 ± 3.1	88.1
Na	(1) 50	40	0	60	133.9 ± 1.9	6.4 ± 1.27	4.7
	(2) 40	100	0	0	24.9 ± 1.0	3.7 ± 0.7	14.8
	(3) 50	25	25	50	4.23 ± 0.51***	2.52 ± 0.5	59.5
K	(1) 70	29	57	14	4.4 ± 0.3	0.52 ± 0.05	11.8
	(2) 40	50	0	50	82.3 ± 3.4	4.7 ± 1.0	5.7
	(3) 75	33	50	17	16.53 ± 2.69	10.38 ± 2.69*	62.8
Na/K	(1) 70	14	43	43	31.8 ± 1.99	5.2 ± 0.59	
	(2) 40	50	50	0	0.3 ± 0.01	0. 5 ± 0.001	
	(3) 63	0	40	60	0.28 ± 0.05	0.18 ± 0.05	
Ca	(1) 80	0	0	100	2.2 ± 0.21	0.4 ± 0.03	18.2
	(3) 63	20	20	60	34.2 ± 1.53***	24.6 ± 4.61***	71.9
Mg	(1) 60	33	0	67	1.3 ± 0.07	0.2 ± 0.02**	15.3
	(3) 50	0	25	75	65.38 ± 11.5	53.8 ± 15.4	82.3
Cu	(1) 70	14	43	43	11.4 ± 1.3	2.8 ± 0.2*	24.5
	(3) 50	0	25	75	0.17 ± 0.02**	0.13 ± 0.03	76

Indices	S	U	C	I	Mesor ± SE	Amplitude ± SE	A/M %
Zn	(1) 60 (3) 62	17 60	0 0	83 40	24.5 ± 0.7 2.11 ± 0.22**	5.6 ± 0.6 1.48 ± 0.32	22.8 70.2
Corticosterone	(1) 70	0	0	100	33.3 ± 2.2**	30.9 ± 2.3**	92.8
Total Percent	(1+2) 61	23	21	56			
Total Percent	(3) 57	19	27	54			

Note: *-$p < 0.05$;**-$p < 0.01$;***-$p < 0.001$ they were calculated comparably with data of intact animals. Mesors and amplitudes were calculated by 100 mg mass of the body the following unites : Na, K (1, 2) ; Ca, Mg (1) mmol/l; Cu, Zn (1) Mmol/l; corticosterone (1) - nmol/l volume of urine ml/hour, Na, K (3) mkmol/hour ; Cu, Mg, Cu, Zn (3) nmol/hour

Discussion and Conclusion

Our results showed that in the healthy subjects the rhythms of electrolytes and trace elements excretion were sinusoidal and circadian. It was stated as an internal synchronization by periods which met the relative stationarity of the biological rhythms. The synchronization by rhythms period was inherent for normal functions of the organism. Our results showed that in cardiovascular pathology beginning from the early stages (IHD 1 and H1) electrolytes and trace elements the excretion rhythms changes took place, which were expressed in the alterations of period, mesor and amplitude in comparison with the data of the healthy subjects.

Thus, the new neuroendocrine status of the organism reorganized the circadian rhythms of water- mineral internal for preservation of relative stationary of the electrolytes and trace elements composition in the internal environment at the early stage of cardiovascular pathology. Those procedure reactions went out slowly in the late stage of the cardiological pathology (IHD2 and H2). The results also showed that in the heart disease patients depending upon the gravity of pathological state, in 31-32% statistically significant rhythms of electrolytes and trace elements excretion were not revealed. We couldn't compare our data with the results of other authors, as similar investigations in cardiology patients hadn't found in the available literature. Thus, the change of period, mesor and amplitude of the rhythms of the electrolytes and trace elements excretion in urine obtained early diagnostic significance. Those data could also help in the organization of pathogenic therapy of the cardiology patients taking into account the temporal structure of water mineral homeostasis.

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