IRSTI 34.03.39 https://doi.org/10.26577/eb-2019-4-b10

N.T. Ablaikhanova, S. Tuleukhanov, M.S. Kulbaeva, L.Zh. Gumarova, G.A. Tussupbekova, Nurzat T. Ablaikhanova, A. Yessenbekova, A. Ydyrys

Laboratory of Chronobiology and Esological, Physiology, Research Institute of Biology and Biotechnology, Al-Farabi Kazakh National University, Kazakhstan, Almaty, e-mail: nurzhanat75@mail.ru

CIRCADIAN RHYTHMS OF THE CARDIOVASCULAR SYSTEM IN PATIENTS WITH DIABETS MELLITUS TYPE 2 IN THE SPRING SEASON

Abstract. The study of the biorhythms of the structure allows for more accurate and friendly evaluation of parameters and dynamics of the time organisms of biological systems. At the time, I was unable to cope with the acute aspiration to study the reproductive system of the reproductive system, or when the pathological disorders came out. In the described terms, biorhythms and time management system are characterized by lability and plasticity of parameters.

At the present time, the simple biological process of the rhythmicity of the simple biomedical process, but also the internal structure of the biorhythmic system, its normal size and degree, are initiated by pathological narrowing of biorhythm. The greater the value of the structure is the presence of rhythms in the adaptation process, as well as in the forming of physiological changes in differential stressful suppressions, in the mornings, and in the saccharide diabetes. Based on the above, it seems relevant to study the chronostructural reorganization of the electrocardiogram rhythms of the body with physiological and pathological changes in groups of healthy people and in patients with type 2 diabetes mellitus in order to assess the degree of influence of diseases on the cardiovascular system of the human body.

Key words: biorhythm, temporary organization, chronostructure, cardiovascular system, type 2 diabetes

Н.Т. Аблайханова, С. Тулеуханов, М.С. Кулбаева, Л.Ж. Гумарова, Г.А. Тусупбекова, Н. Аблайханова, А. Есенбекова, А. Ыдырыс

Биология және биотехнология мәселелері ғылыми зерттеу институты, Хронобиология және экологиялық физиология зертханасы, әл-Фараби атындағы Қазақ ұлттық университеті, Қазақстан, Алматы қ., e-mail: nurzhanat75@mail.ru

Жылдың көктемгі маусымында дені сау және ауру адамдардағы 2 типті қант диабеті кезіндегі кардиожүйенің циркадиандық биоырғағы

Аңдатпа. Бұл мақалада биоырғақтардың құрылымын зерттеу биологиялық жүйелердің уақытша құрылымының динамикасы мен көрсеткіштерінің нақты және шынайы бағалауға көмектесетіндігі қарастырылған. Осыған орай экзо-, эндогендік факторлармен қоса патологиялық бұзылыстарға жауап реакциясы ретінде тірі ағзалардың уақытаралық ұйымдасуын зерттеу ерекше өзіндік өзектілігін көрсетеді. Белгіленген жағдайларда тірі жүйелердің уақытаралық ұйымдасуы мен биоырғағы жалпы көрсеткіштерінің тұрақсыздығымен, икемділігімен сипатталады.

Қазіргі таңда биологиялық процестердің ырғақтылығын ғана сипаттау жеткіліксіз болып табылады, жүйе ретінде биоырғақтардың ішкі құрылымын, олардың қалыпты өзгергіштігінің шегін, патологиялық ырғақтың басталу шектеулерін де анықтауды қажет етеді. Бейімделу үрдістерінде, әртүрлі стресс тудырушы әсерлерден, соның ішінде қант диабетінде физиологиялық өзгерістердің қалыптасуында ағза ырғағының құрылымының үлкен мәні бар. Жоғарыда айтылғандарды ескере отырып, адам ағзасының жүрек-қан тамырлар жүйесіне қант диабеті ауруының тигізетін әсерін бағалау мақсатымен дені сау адамдар тобының және 2-типтегі қант диабетімен ауырған науқастардың физиологиялық және патологиялық өзгерістері туындағанда ағзаның электрокардиограммалық ырғағының хроноқұрылымдық көрсеткіштерінің қайта құрылуын анықтауға арналған зерттеу жұмысы өзінің өзектілігін көрсетеді.

Түйін сөздер: биоырғақ, уақытаралық ұйымдасуы, хроноқұрылымдық, жүрек-қан тамырлар жүйесі, 2-типтегі қант диабеті.

Н.Т. Аблайханова, С. Тулеуханов, М.С. Кулбаева,
Л.Ж. Гумарова, Г.А. Тусупбекова, Н. Аблайханова, А. Есенбекова, А. Ыдырыс

Лаборатория хронобиологии и экологической физиологии,
Научно-исследовательский институт проблем биологии и биотехнологии,
Казахский национальный университет имени аль-Фараби,
Казахстан, г. Алматы, e-mail: nurzhanat75@mail.ru

Циркадинные ритмы сердечно-сосудистой системы у здоровых и больных сахарным диабетом 2 типа в весенний сезон года

Аннотация. Исследование структуры биоритмов позволит более точно и достоверно оценить параметры и динамику временной организации биологических систем. При этом необходимо почеркнуть особую актуальность изучения временной организации живой системы при реакции на воздействие, или когда в ней происходят патологические нарушения. В указанных условиях биоритмы и временная организация системы в целом характеризуются лабильностью и пластичностью своих параметров.

В настоящее время недостаточно простого признания ритмичности биологического процесса, необходимо еще и знать внутреннюю структуру биоритма как системы, границы ее нормальной изменчивости и те пределы, за которыми уже начинаются патологические нарушения биоритма. Большое значение структура ритмов организма имеет в процессах адаптации, а также в формировании физиологических измененийй при различных стрессовых воздействиях, при заболеваниях, в том числе и сахарном диабете. На основании вышеизложенного нам представляется актуальным изучение хроноструктурной перестройки ритмов электрокардиограммы организма при физиологических и патологических изменениях в группах практически здоровых людей и у пациентов с заболеванием сахарный диабет 2-го типа с целью оценки степени влияния заболеваний на сердечно-сосудистую систему организма человека.

Ключевые слова: биоритм, временная организация, хроноструктура, сердечно-сосудистая система, сахарный диабет 2 типа.

Abbreviations

ECG – electrocardiogram, HRV – heart rate variability, HR – heart rate, BP – blood pressure

Introduction

The analysis of the temporal organization of the body's function should, to a significant extent, be based on the study of chronostructural parameters of rhythms: period, amplitude, mezor, acrophase. These parameters reflect the structural organization of the biorhythm in time and space and in their totality represent a certain system [1].

When studying biorhythms, preliminary planning and organization of observations and experiments are extremely important. It is believed that in order to assert that there is a rhythm, the researcher must have at least four measurement points at different times in each of the successive three periods. It is absolutely not enough to conduct observations for only one day (to identify the daily rhythm) and to extrapolate the results for subsequent periods of time, since all the parameters of the rhythm – phase, amplitude, mezor – vary from day to day [2, 3].

F. Halberg suggested that when studying daily rhythms, the experimental data be approximated by the first member of this series – a harmonica with a period of 24 hours. The approximation of individual daily curves by harmonics is the first step in constructing a model of bio-rhythms using the Kosinor method. When studying chronobiological information, many researchers reject modeling and apply methods of direct analysis of experimental data. Thus, according to the many-day observations (physiological, biophysical indicators were measured at the same time 8-10 times per day), the following values are calculated: the position and magnitude of the maximum and minimum values of the indicator, the difference between the maximum and minimum values of the indicator, the length of the ascending and descending branches, the size of the wandering zone acrophase. Great importance in assessing the biorhythm is attached to the visual comparison of chronograms [4].

In this method, an attempt was made to combine a detailed study of chronograms with the merits of approaches using modeling: generalization and compact presentation of experimental data, the ability to predict in new conditions [5].

Seasonal and other adaptive types of rhythms are also not a simple reaction to cyclical changes in the habitat, but are characterized by a certain endogeneity. Consideration of physiological rhythms is necessary when drawing up a rational mode of work and rest of a person, when choosing the time of taking medicines, especially hormonal drugs. Physiological rhythms have a certain diagnostic value in the clinic, the physiology of labor and sports medicine: in various diseases and overwork they are disturbed [6,7].

Many human diseases are characterized by unusual and complex dynamics. The analysis of the mechanisms underlying such diseases is inevitably associated with a theoretical analysis of the observed dynamics. Methods for studying these problems consist in the formulation of theoretical and biological models of the disease. A far-reaching goal of researchers is to help develop new diagnostic and therapeutic strategies in treating people [8].

One of the informative methods that determine the biorhythmic changes in the functional state of the cardiovascular system is the method of daily monitoring according to Holter. It allows you to record the daily dynamics of the heart rate, electrocardiogram indicators, which significantly increases the detection of non-permanent temporal changes. The circadian profile of the heart rhythm, evaluating changes in the daily dynamics of the pulse, was used in the studies of LM. [9].

Makarov to clarify its clinical significance in the diagnosis of many dangerous diseases. She calculated the circadian profile as the ratio of the average heart rate during the waking period (from 07 to 22 hours) to the average heart rate during the night sleep period (from 23 to 06 hours). According to the calculations of the QI indicator, it is possible to make separately the average day and night values of the HR or RR intervals in healthy subjects and patients aged 2 to 99 years, both according to the results of the classical Holter monitoring and blood pressure monitoring. The research results showed high stability of QI in all groups of healthy subjects, regardless of gender, age and type of equipment used. The value of QI, based on its calculation based on the results of 20 studies, combining the results of daily monitoring in 7870 healthy subjects from 10 to 79 years old, practically does not differ from the standard parameters (1.32 ± 0.06) and averages 1.33 ±0, 05 [10].

L.G. Shipova and co-workers conducted a survey of the circadian profile in children, which made it possible to determine its normative values that do not depend on age and gender [11].

According to the study of the daily rhythm of the heart in healthy individuals, it is also possible to calculate the difference between the average night and day RR intervals: Night / day difference (Ndd), a parameter for the temporal analysis of heart rate variability, which can be used to analyze the circadian rhythm of heart rate. A significant correlation of the Night / day difference is noted with the night level of the heart rate (r = -0.61). At the same time, no reliable interdependencies were found between the parameters of heart rate and QI, nor was the close dependence of this indicator on the initial level of heart rate found [12].

High variability in age and physiological fluctuations of the mean heart rate (sinus bradycardia or tachycardia), even in healthy subjects, leads to the absence of stable regulatory standards in the assessment [13].

This method turned out to be informative for children and for adults. Galeev et al. studied the mean value of the N – N intervals (M) in children 6–16 years of age, which increased with age (p <0.0001), varying in waves from year to year. They suggested using the obtained values in practice as normative [14].

The functional state of the cardiovascular system varies significantly throughout the seasons. The maximum heart rate (HR), blood pressure (BP), myocardial contractile function (MFM) and the minute volume of blood circulation in healthy people are observed in the winter. The greatest number of vascular accidents with coronary heart disease falls in the autumn months [15, 16].

Analysis of the distribution of the incidence of coronary artery disease with varying degrees of severity of angina pectoris by seasons showed that in the spring and winter periods there was an increase in the number of patients with functional class II stenocardia, and in the summer months their number sharply decreases. Such variability in the course of the disease is accompanied by seasonal changes in the indicators of the functional state of the cardiovascular system. Seasonal study of daily periodicals of heart rate as an integral indicator of the adaptive processes of the cardiovascular system and the whole organism in patients with coronary artery disease revealed the deterioration of temporary adaptation processes in transitional periods of the year: violations of the daily pulse rhythm with the same frequency were encountered in spring and autumn and less often in summer and winter [17, 18].

The study of seasonal phenomena is of undoubted interest in terms of their participation in the general complex of biological rhythms characteristic of living organisms. In addition, the study of seasonal rhythms pursues independent goals, which are associated with the development of effective ways of controlling biological processes occurring at the level of organisms, etc. [19, 20].

A promising direction of the search is the study of seasonal fluctuations of the hypothalamic-pituitary-neurosecretory system, which plays an important role in mobilizing the adaptive reactions of the body in response to an abrupt change of environment. Seasonal rhythm is characteristic of most physiological processes, including the release of hormones by the adrenal glands, depending on the season of the year and the time of day. The daily fluctuations of hormones themselves, their chronostructure, react sensitively to stress [21].

However, it remains an open question about the influence of the seasons of the year on the chronostructural changes in the indices of the cardiovascular system in patients with type 2 diabetes mellitus.

Materials and metods

2.1, 2.2, 2.3 Under supervision were people of both sexes aged 40 to 62 years. A total of 11 people were examined, 3 of them in the control group, without diseases of the cardiovascular and endocrine systems, and 8 people with type 2 diabetes, with experience from 4 to 10 years. A total of 1056 measurements were taken.

Continuous daily electrocardiogram (ECG) recording was performed on a SHILLER MT-200, HOLTER-EKG V2.10 apparatus. A 3-channel cardiograph was used, using bipolar lead systems (one positive and one negative lead) for each channel (lead V5, V2, V3). Channel 1 approximately corresponds to the modified lead V5, channel 2 approximately corresponds to V2, and channel 3 corresponds to V3. In addition to the generally accepted analysis of ST segment changes, the trend of the latter was assessed during the day, at which the angle of ST segment decline relative to the isoline hourly was analyzed. ECG recording was performed using a special portable recorder, which the patient carries with him (at the waist).

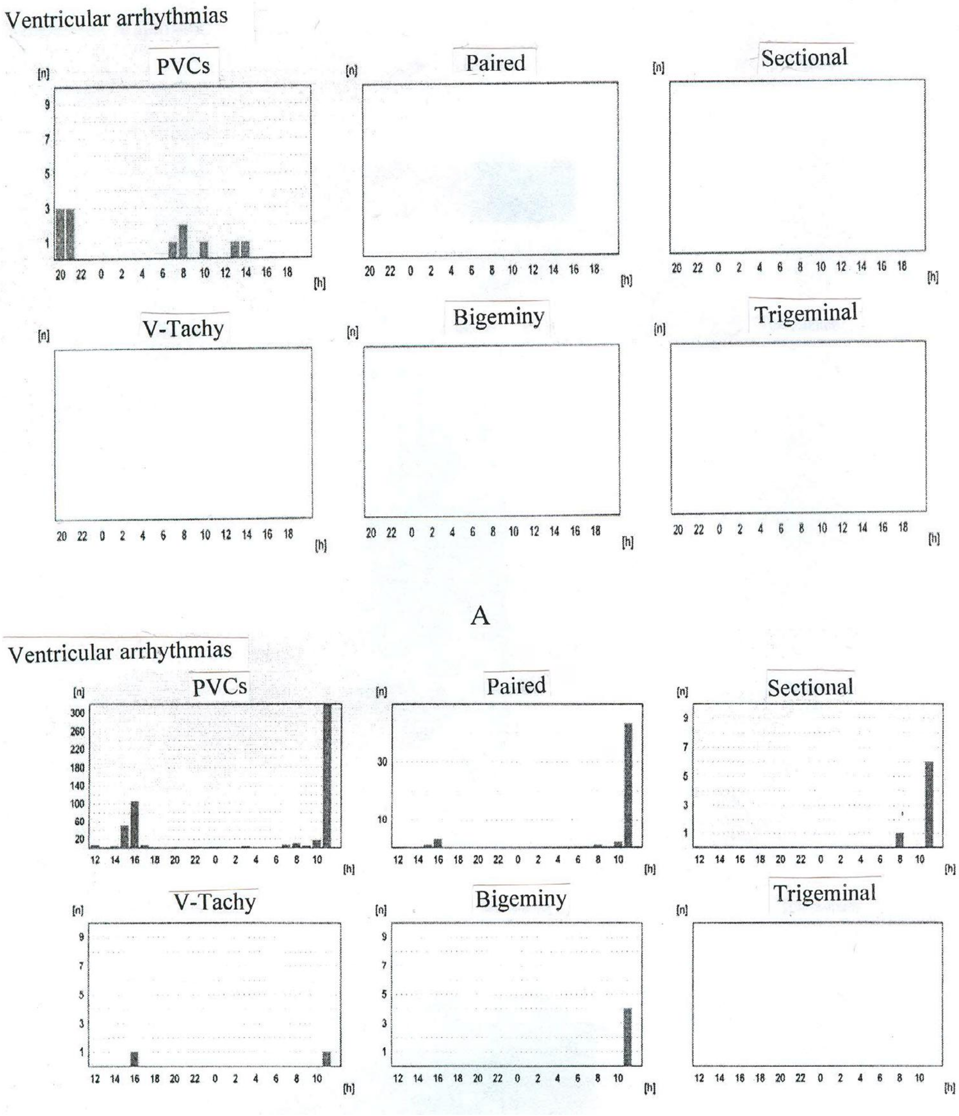
Analysis of the daily ECG for the detection of arrhythmias and heart rate variability (HRV) by heart rate (HR) was performed using the SHILLER MT-200 program. HRV scores were reviewed in accordance with the standards of the European Society of Cardiology and the North American Electrophysiological Society.

The chronostructural parameters of the daily dynamics of the heart rate were evaluated, as well as the parameters of HRV by RR (MC), only time intervals between normal QRS complexes (NN-intervals) were used, registrations were divided into five-minute intervals for the analysis of HRV. Statistical indicators of heart rate variability, spectral analysis, Kosinor analysis were used.

Results and discussion

The most important problem of modern diabetology is the development of new, more effective methods of preventing and treating type 2 diabetes, designed to reduce the growth rate of the number of patients in the population, as well as significantly reduce the risk of developing micro- and macrovascular complications, polyneuropathy, increase the life expectancy of patients and minimize socio-economic losses. Based on data from a retrospective analysis of many large-scale, international studies in the field of diabetes, it is stated the need for effective multifactorial management of numerous disorders developing in type 2 diabetes, which is associated with large objective and subjective difficulties. New accents and goals for the correction of metabolic and vascular abnormalities are noted, an understanding of the role of the pathogenetic factors of the disease is reviewed, the priority of a multi-pronged interventional approach is emphasized. Modern tactics of managing patients with type 2 diabetes should be based on a deep understanding of the mechanisms of its development in order to correct key pathogenetic defects, to achieve early, tough and at the same time safe glycemic control, as well as long-term correction of metabolic and vascular abnormalities.

There is a presence of HES at night, morning and daytime in the group of healthy subjects (Figure 1-A), regardless of gender. The HPS value, based on our calculation based on the results of three replications of studies combining the results of daily monitoring in healthy subjects from 40 to 62 years old in spring, practically does not differ from the previously determined standard parameters and averages 1.5 ± 0.3. In a study by J. Freitas et al. a high reproducibility of the daily structure of the heart rhythm is shown, even when changing periods of sleep and wakefulness in shift workers [22, 23].



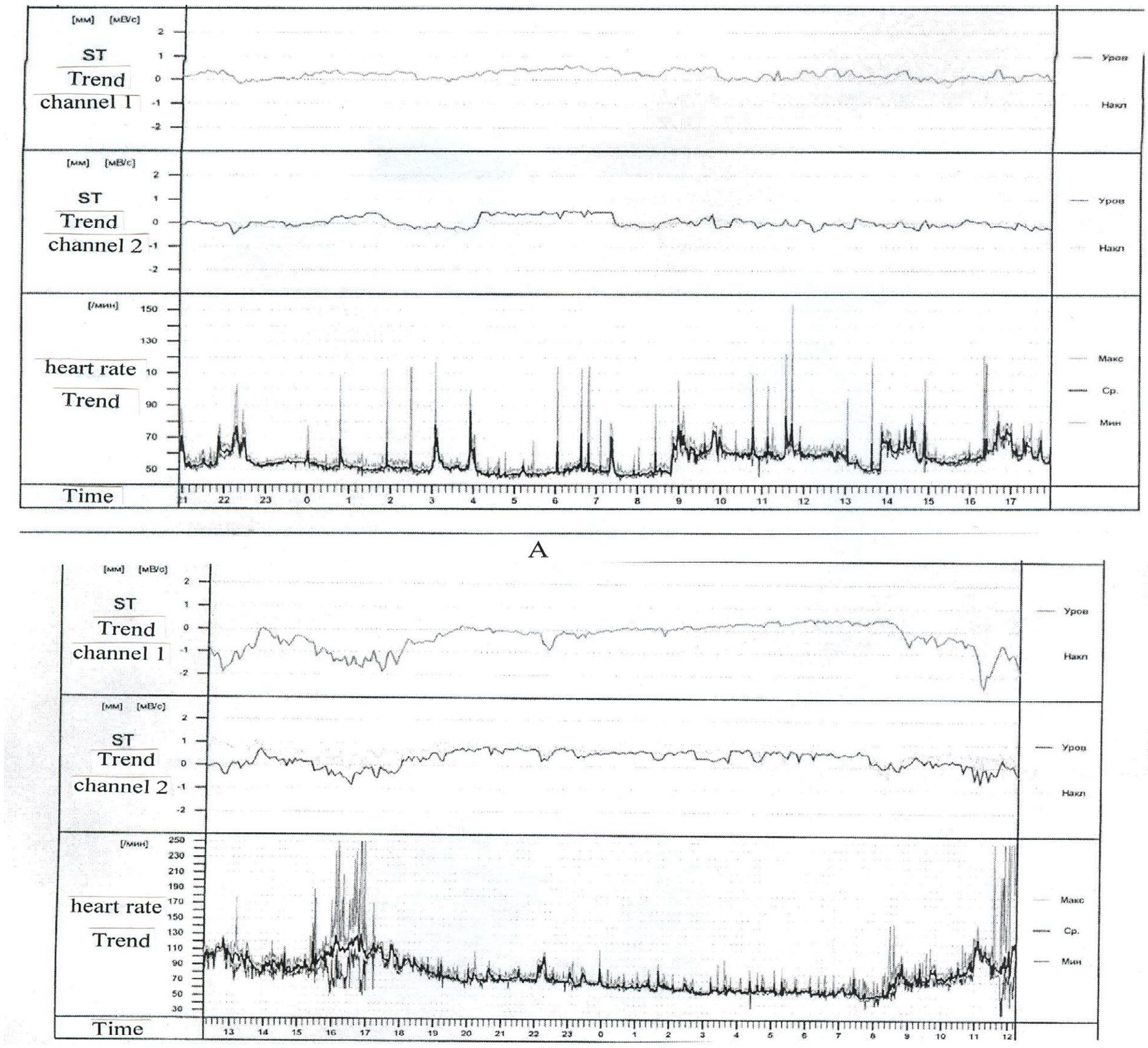
B

Figure 1 – The daily dynamics of ventricular arrhythmia in a person's heart is normal (A) and in diabetes mellitus (B) in the spring period of the year

Estimated indicators of paired, group, life time, bigeminia and trigeminia in healthy people in the spring period of the year are not detected (Figure 1 A).

Analysis of ventricular arrhythmias in sick people in the spring indicates the following, for example, the HPS values are found in the morning and noon time of the day, absent at night, the HES parameters vary 10 to 300 ± 2.4, much higher than normal. The parameters paired, group, F Takhi, bigeminy are found mainly in the morning, and there are no indicators of trigeminia (Figure 1 V). Comparative analysis of ventricular arrhythmias in healthy and sick people with type 2 diabetes suggests a striking difference between them (Figure 2 A, B).

We also established daily rhythms of ST and heart rate trends in humans in normal conditions and in diabetes mellitus in the spring period of the year. ST trend indicators for the first channel during the day are above zero, and for the second channel it is equal to above zero, and the HR trend parameters for 24 hours vary from 45 to 86 and with an increase in the HR value in the morning, received and night hours. And the same indicators of ST and heart rate in sick people had the following values: Trend ST of the first channel is mainly below zero, and in the second channel it is mostly above zero.



B

Figure 2 – The daily dynamics of ST and HR trends in the human heart is normal (A) and in diabetes mellitus (B) in the spring period of the year

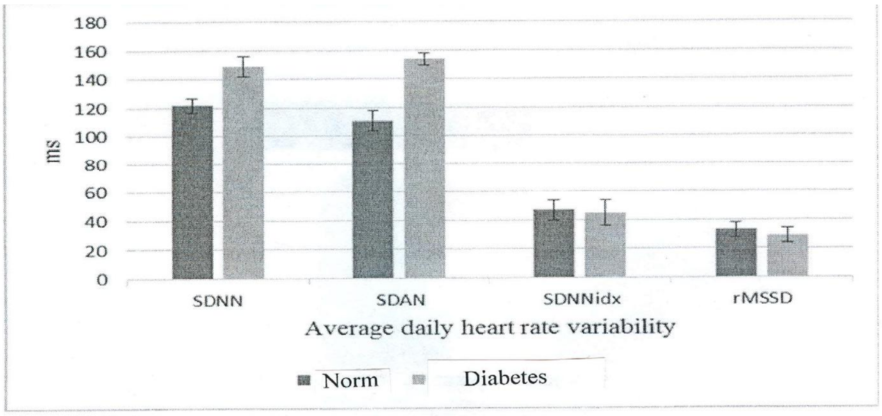
The parameters of the HR trend in patients varied from 60 to 130, with peaks in the morning and afternoon hours of the day (Figure 2 B). The results obtained indicate a difference in ST and heart rate indicators in sick people relative to the norm.

Figure 2 presents a comparative analysis of the average daily and average margins of human heart rate variability in normal conditions and in cases of diabetes in the spring period of the year. The figures show that the average daily SDNN (ms), SDANN values in healthy people are lower, and the SDNN idx (ms) and r MSSD (ms) values are higher than in sick people. And the average indicators have the following relationship between normal and pathological. Thus, the SDNN (mc) indices are equal to each other, the SDANN and SDNN idx (msec) values are normally less than in pathology, and r MSSD (ms), on the contrary, and the norm is higher than in sick people.

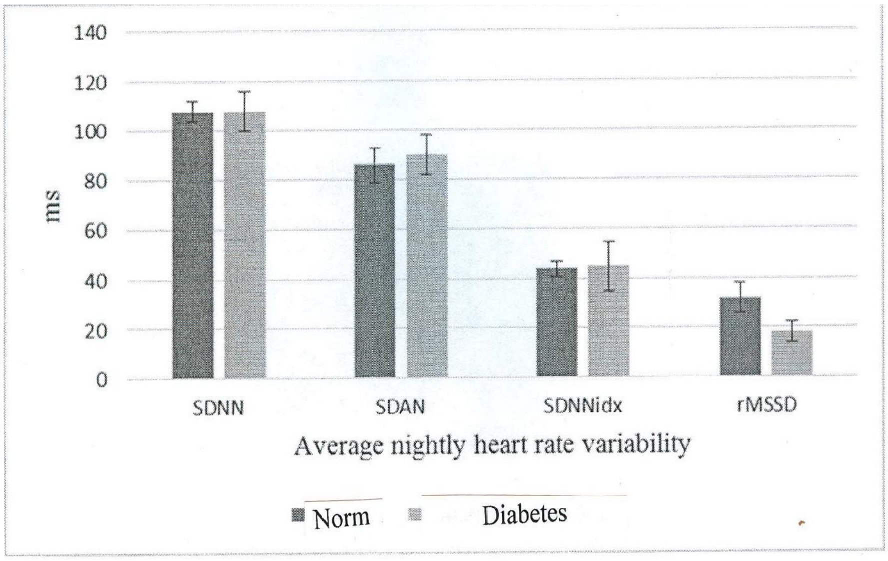
And figures 3.4 show average daily heart rate variability in healthy people and in patients with type 2 diabetes. As can be seen from the figure, daily indices of NN 50 in healthy people are higher than in patients, and indicators of NN 100 and NN 200, on the contrary, are normally less than in pathology. A nightly indicators NN 50, NN 100 and NN 200 in healthy people is higher than in patients with diabetes.

Thus, we have identified distinctive signs in the daily parameters of the cardiovascular system in patients with type 2 diabetes, relative to the norm.

Figures 5 and 6 show the indicators of the autospectra of the daily dynamics of the heart rate and the QRS complex in healthy and sick people with type 2 diabetes in the spring period of the year. From the figures it is clear that the daily rhythms of the heart rate and the QRS complex consists of ultradian rhythms, since the maximum values of the autospectra fall at 14 hours. and 08 hours



A



B

Figure 3 – Average daily (A) and average (V) indicators of heart rate variability in humans in normal and diabetes in the spring period of the year

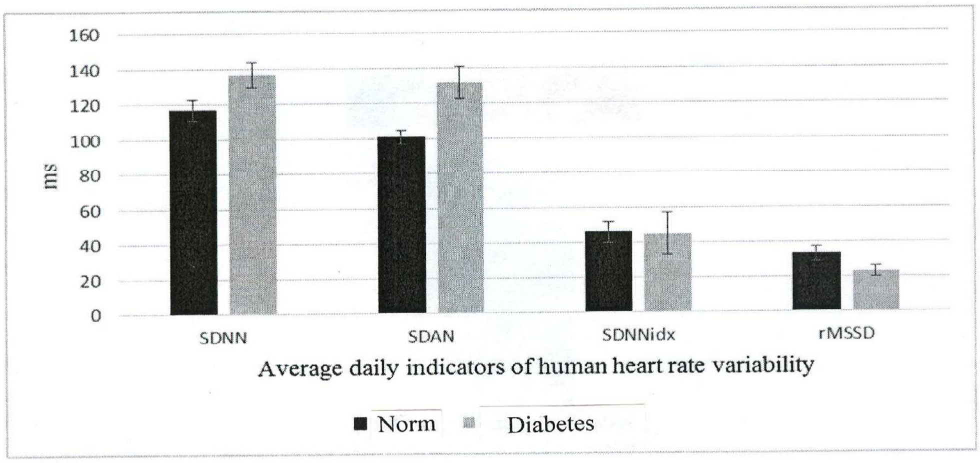


Figure 4 – Average daily indicators of human heart rate variability in normal and diabetes in the spring period of the year

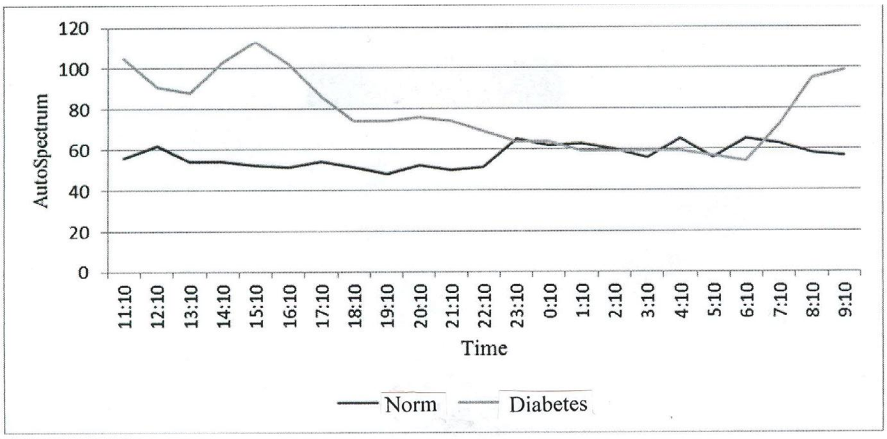


Figure 5 – Autospectrum of the daily dynamics of the heart rate in healthy and sick people in the spring period of the year

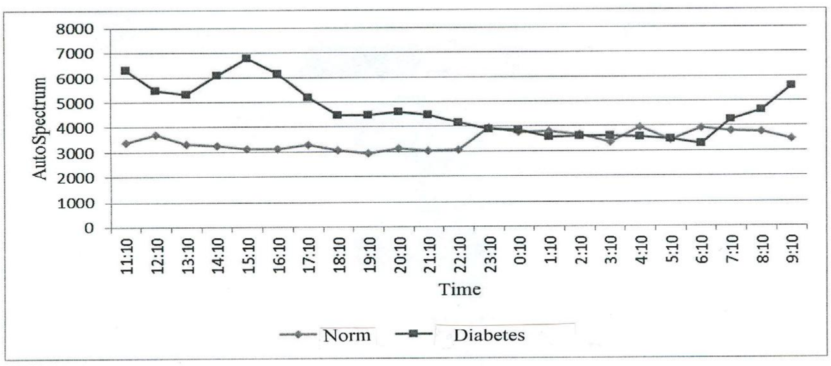


Figure 6 – Autospectrum of daily dynamics of the QRS complex in healthy and sick people in the spring period of the year

The cosinor analysis allowed us to establish the values of the chronostructural parameters of the rhythms of the cardiovascular system of a person in normal and pathological conditions.

Thus, the daily rhythms of cardiac systems at 24 hours are absent both in normal conditions and in pathology. Mezor is normally equal to 56, and with pathology 78, the amplitude is normal – 12 (07 ÷ 17), with pathology – 111 (51 ÷ 172), and acrophase is normal – 05 hours. 10 min., And for pathology, 14 h. 10 min. [24].

Heart rate variability (HRV) data in normal and pathological conditions showed that, according to the results of daily monitoring, less than half of the analyzed parameters of heart rate variability remain stable. Of the 12 parameters analyzed, statistically significant differences were identified by 9 parameters, and by the following indicators: SDNN idx (ms), pNN 200%, the differences in statistical changes are insignificant (Table 1)

The SDNN idx parameter (standard deviation of NN intervals), reflecting the integral effects of the sympathetic and parasympathetic divisions of the ANS, also slightly decreased overall over the day in case of pathology, while the reliability of changes in its night and day indices was low, i.e. unreliable. The parameter r MSSD (ms), is an indicator of the activity of the parasympathetic link of the vegetative regulation, decreases at night, especially in case of pathology [25].

Table 1 – Heart rate variability in humans in normal and diabetes in the spring period of the year

Parameters	Norm			Diabetes		
	day	night	twenty-four hours	day	night	twenty-four hours
1	2	3	4	5	6	7
Witness NN, %	99,9±1,6	100,0±2,4	100,0±2,8	88,2±5,5	99,7±4,67	91,8±5,34
Medium NN,ms	1002±16,23	1120±19,34	1049±18,06	708±25,4	937±36,3	784±32,2
SDNN,ms	122±5,68	108±4,7	117±6,37	149±7,42	108±8,75	137±7,86
SDAN,ms	111±7,5	86±3,64	101±6,42	154±9,5	90±10,4	132±12,3
SDNNidx ms	47±3,22	44±5,56	46±4,45	45±6,78	45±5,67	45±4,89
rMSSD, ms	33±2,84	32±3,02	33±6,5	29±4,5	18±3,9	26±6,2
NN50	1279±543,2	719±78,6	1998±463,7	1254±359,6	320±45,8	1574±467
pNN50,%	3,0±0,24	2,5±0,54	2,8±0,76	1,8±0,85	0,9±0,08	1,5±0,68
NN100	217±66,57	134±58,9	351±79,5	376±82,4	24±4,65	400±34,3
pNN100,%	0,5±0,03	0,5±0,07	0,5±0,04	0,5±0,02	0,1±0,05	0,4±0,07
NN200	131±77,3	79±26,5	210±95,7	170±78,8	7±1,6	177±78,6
pNN200,%	0,3±0,08	0,3±0,04	0,3±0,02	0,2±0,04	0,4±0,05	0,2±0,04
** p ≤ 0,01; – *p ≤ 0,05.						

The sum of all adjacent NNC intervals with oscillations over 50 ms (NN 50) and its share, calculated from the total number of NN intervals, decreased slightly during the day, and significantly at night, and also for the whole day. The greatest changes were found in pathology exchanged in terms of HRV parameters: NN medium (ms), SDNN (ms), SDANN (ms), NN 50, p NN 50%, NN 100, NN 200. Reduction in r MSSD (ms), p NN 50 and NN 50, which are markers of the parasympathetic nervous system, may indicate a suppression of its activity and a sharp predominance of sympathetic activity. The great significance of changes at night in a number of indicators may indirectly indicate the effect of pathology on night sleep. There is a linear correlation between the increase in the incidence of diabetes and the increase in CVD complications. There is every reason to assume that in the next 20 years the proportion of patients with type 2 diabetes in the structure of cardiovascular complications will increase [26].

Conclusion

Excessive increase in blood glucose level after a meal, on the one hand, is the earliest and most adequate diagnostic sign of type 2 diabetes, on the other hand, has an unfavorable prognostic value in terms of cardiovascular complications, which confirms one of the latest studies in this area – DECODE (Diabetic Epidemiology Collaborative Analysis Of Diagnostic Criteria in Europe) Effective management of type 2 diabetes today can be thought of as a set of measures aimed not only at compensating carbohydrate metabolism, but also at eliminating other risk factors for cardiovascular disease – hypertension and dyslipidemia.

Thus, we have established daily rhythms of indicators of the cardiovascular system of a person in health and pathology in the spring period of the year.

Conflict of interest

All authors have read and are familiar with the content of the article and do not have a conflict of interest.

References

1 Scheffer I. E. A century of mitochondrial research: achievements and perspectives. Mitochondrion. // – 2001. – vol. 1, № 1. – P. 3-31.

2 Den Besten. G., van Eunen. K., Groen. A.K. ,Venema. K., Reijngoud. D.J., Bakker. B.M. The role of short-chain fatty acids in the interplay between diet, gut microbiota, and host energy metabolism // J. Lipid Res. -2013. №54. – P. 2325–2340.

3 Stern M. P. Diabetes and cardiovascular disease. The «common soil» hypothesis. Diabetes // – 1995. – vol. 44. – P. 369-374.

4 Халберг Ф. Временная координация физиологических функций // Биологическое часы. Москва. – 1964. – С. 475-509.

5 Camp. H.S., Ren. D., Leff. T. Adipogenesis and fat-cell function in obesity and diabetes // Trends Mol. Med. – 2002. №8. – P. 442–447.

6 Inzucchi, S.E., Bergenstal, R.M., Buse, J.B., Diamant, M., Ferrannini, E., Nauck, M., Peters, A.L., Tsapas, A., Wender, R., Matthews, D.R. Management of hyperglycemia in type 2 diabetes: A patient-centered approach // Diabetes Care. – 2012. №35. – P. 1364–1379.

7 Takeshi K., Daisuke Y., Nobuya I. Circadian rhythms and diabetes Journal of Diabetes Investigation //J Diabetes Investig. – 2011. №2(3). – P.176–177.

8 Khan. S., Jena. G. Sodium butyrate reduces insulin-resistance, fat accumulation and dyslipidemia in type-2 diabetic rat // A comparative study with metformin. Chem. Biol. Interact. – 2016. №254 – P. 124–134.

9 Mooradian. A.D. Dyslipidemia in type 2 diabetes mellitus // Nat. Clin. Pract. Endocrinol. Metab. -2009. №5. –P.150–159.

10 Yu J. Z., Rodrigues B., McNeill J. H Intracellular calcium levels are unchanged in the diabetic heart // Cardiovasc-Res. – 1997. – vol. 34. – №1. – P. 91-98.

11 Ziegler D., Hanefeld M., Ruhnau K. J. Treatment of symptomatic diabetic polyneuropathy with the antioxidant a-lipoic acid // Diabetes Care.- 1999. – V. 22. – P. 1296-1301.

12 Handelsman Y., Mechanick JI., Blonde L., Grunberger G., Bloomgarden ZT., Bray GA., American Association of Clinical Endocrinologists medical guidelines for clinical practice for developing a diabetes mellitus comprehensive care plan //. et al; AACE Task Force for Developing a Diabetes Comprehensive Care Plan. Endocr Pract. – 2011. №17. –P. 53.

13 Lin. H.V., Frassetto. A., Kowalik. E.J., Nawrocki. A.R.; Lu. M.M.. Kosinski. J.R. , Hubert. J.A., Szeto. D., Yao.X., Forrest.G. Butyrate and propionate protect against diet-induced obesity and regulate gut hormonesvia free fatty acid receptor 3-independent mechanisms. PLoS ONE. – 2012. –P.7.

14 Zimmet P. The burden of type 2 diabetes: are we doing enough?. Diabetes Metabolism // – 2003. – Vol. 29 (6), – P. 619-620.

15 Агаджанян Н.А. Стресс и терапия адаптации // Оренбург: ИПК ГОУ ОГУ.- 2005. – С.190

16 Агаджанян Н.А., Петров В.И., Радыш И.В. и др. Хронофизиология, хронофармокология и хронотерапия // М.: Волгоград. – 2005. – С.335.

17 Хетагурова Л.Г. Патофизиология десинхронозов // Владикавказский медико-биологический вестник. – 2005. – Т. 5. – № 9-10. – С. 32-40.

18 Pottie K., Jaramillo A., Lewin G., Dickinson J., Bell N., Brauer P. Recommendations on screening for type 2 diabetes in adults //CMAJ. – 2012. №184(15). – P.1687-96.

19 Hamman, R.F., Wing, R.R., Edelstein, S.L., Lachin, J.M., Bray, G.A., Delahanty, L., Hoskin, M., Kriska, A.M.. Effect of weight loss with lifestyle intervention on risk of diabetes // Diabetes Care. – 2006. – P. 2102–2107.

20 Rahman M., Simmons R.K., Hennings S.H., Wareham N.J., Griffin S.J. Effect of screening for type 2 diabetes on population-level self-rated health outcomes and measures of cardiovascular risk // Diabet Med. – 2012. №29(7) P. 886-92.

21 Gumarova L., Germaine Gornelissan, Ablayhanova N. Circasepran rhytyms of motion activity// International Journal of Biology and Chemistry 10, -2017. №2, P.19-22.

22 Барбараш Л.С., Барбараш О.Л., Барбараш Н. Хронбиологические аспекты кардиологии и кардиохирургии // Кемерово: Летопись. – 2001. – С.178.

23 Radonjic. M., Wielinga. P.Y., Wopereis. S., Kelder. T., Goelela. V.S., Verschuren. L., Toet. K., vanDuyvenvoorde. W., Stroeve. J.H., Cnubben. N. Differential effects of drug interventions and dietary lifestyle in developing type 2 diabetes and complications // A systems biology analysis in ldlr−/− mice. PLoS ONE. – 2013. – P.8.

24 Довголис С.А., Фомина И.Г., Улыбышева М.А. и др. Исследование суточный динамики различных проявлений нарушения ритма сердца у больных ИБС с мерцательной и хронической сердечной недостаточностью ФК II-III NYHA // Здоровье и образование в XXI веке. Концепции болезней цивилизации: материалы Международного конгресса. – Москва. – 2007. – С. 725-727.

25 Карп В.П., Довголис С.А., Фомина И.Г., Улыбышева М.А. Исследование суточной динамики различных проявлений нарушения ритма сердца у больных с мерцательной аритмией и хронической сердечной недостачностью // Материалы 4-ой научно-практической конференции "Новые технологии в рекреации здоровья населения". – Владикавказ. – 2007. – С. 75-78.

26 Писарук А.В., Шатило В.Б., Лишневская В.Ю. Суточные колебания вариабельности ритма сердца при старении // Ин-т геронтологии АМН Украины. – Киев. – 2005. – С. 9-11.

References

1 Scheffer I. E (2001) A century of mitochondrial research: achievements and perspectives. Mitochondrion. – vol. 1, № 1. – pp. 3-31.

2 Den Besten. G., van Eunen. K., Groen. A.K. ,Venema. K., Reijngoud. D.J., Bakker. B.M. (2013) The role of short-chain fatty acids in the interplay between diet, gut microbiota, and host energy metabolism // J. Lipid Res. -. №54. –P. 2325–2340.

3 Stern M. P. (1995) Diabetes and cardiovascular disease. The «common soil» hypothesis. Diabetes.- vol. 44.- pp. 369-374.

4 Halberg F. (1964) Vremennaya koordinatsiya fiziologicheskikh funktsiy [Time coordination of physiological functions]. Biological clock. Moscow, pp. 475-509.

5 Camp. H.S., Ren. D., Leff. T. (2002) Adipogenesis and fat-cell function in obesity and diabetes // Trends Mol. Med. –. №8. –P. 442–447.

6 Inzucchi, S.E., Bergenstal, R.M., Buse, J.B., Diamant, M., Ferrannini, E., Nauck, M., Peters, A.L., Tsapas, A., Wender, R., Matthews, D.R. (2012) Management of hyperglycemia in type 2 diabetes: A patient-centered approach // Diabetes Care. -№35.-P.1364–1379

7 Takeshi K., Daisuke Y., Nobuya I. (2011) Circadian rhythms and diabetes Journal of Diabetes Investigation //J Diabetes Investig. –№2(3). – P.176–177.

8 Khan. S., Jena. G. (2016) Sodium butyrate reduces insulin-resistance, fat accumulation and dyslipidemia in type-2 diabetic rat // A comparative study with metformin. Chem. Biol. Interact. –. №254 -P.124–134.

9 Mooradian. A.D. (2009) Dyslipidemia in type 2 diabetes mellitus // Nat. Clin. Pract. Endocrinol. Metab. -№5. –P.150–159.

10 Yu J. Z., Rodrigues B., McNeill J. H.. (1997) Intracellular calcium levels are unchanged in the diabetic heart // Cardiovasc-Res. – vol. 34.-№1. – pp. 91-98.

11 Ziegler D., Hanefeld M., Ruhnau K. J. (1999) Treatment of symptomatic diabetic polyneuropathy with the antioxidant a-lipoic acid. Diabetes Care, -V.22. – pp.1296-1301.

12 Handelsman Y., Mechanick JI., Blonde L., Grunberger G., Bloomgarden ZT., Bray GA., (2011) American Association of Clinical Endocrinologists medical guidelines for clinical practice for developing a diabetes mellitus comprehensive care plan //. et al; AACE Task Force for Developing a Diabetes Comprehensive Care Plan. Endocr Pract. – №17. –P. 53.

13 Lin. H.V., Frassetto. A., Kowalik. E.J., Nawrocki. A.R.; Lu. M.M.. Kosinski. J.R. , Hubert. J.A., Szeto. D., Yao.X., Forrest.G. (2012) Butyrate and propionate protect against diet-induced obesity and regulate gut hormonesvia free fatty acid receptor 3-independent mechanisms. PLoS ONE.. –P.7.

14 Zimmet, P. (2003) The burden of type 2 diabetes: are we doing enough?. Diabetes Metabolism, – Vol. 29 (6), P.619 – 620.

15 Agajanyan N. (2005) Stress i terapiya adaptatsii [Stress and adaptation therapy] Orenburg: IPK GOU OG, P.190

16 Agadzhanyan N.A., Petrov V.I., Radysh I.V. et al. (2005) Khronofiziologiya, khronofarmokologiya i khronoterapiya [Chronophysiology, chronopharmacology and chronotherapy] M .: Volgograd, P.335.

17 Khetagurova L.G. (2005) Patofiziologiya desinkhronozov [Pathophysiology of desynchronosis]. Vladikavkaz Biomedical Herald, – Vol. 5. – № 9-10. pp. 32-40.

18 Pottie K., Jaramillo A., Lewin G., Dickinson J., Bell N., Brauer P. (2012) Recommendations on screening for type 2 diabetes in adults //CMAJ. –№184(15). – P.1687-96.

19 Hamman, R.F., Wing, R.R., Edelstein, S.L., Lachin, J.M., Bray, G.A., Delahanty, L., Hoskin, M., Kriska, A.M. (2006) Effect of weight loss with lifestyle intervention on risk of diabetes // Diabetes Care.- P. 2102–2107.

20 Rahman M., Simmons R.K., Hennings S.H., Wareham N.J., Griffin S.J. (2012) Effect of screening for type 2 diabetes on population-level self-rated health outcomes and measures of cardiovascular risk // Diabet Med.- №29(7) P. 886-92.

21 Gumarova L., Germaine G, Ablayhanova N.T. (2017) Circasepran rhytyms of motion activity. International Journal of Biology and Chemistry 10, №2, pp.19-22.

22 Barbarash LS, Barbarash OL, Barbarash N. (2001) Khronbiologicheskiye aspekty kardiologii i kardiokhirurgii [Chronbiological aspects of cardiology and cardiac surgery] Kemerovo: Chronicle, P. 178.

23 Radonjic. M., Wielinga. P.Y., Wopereis. S., Kelder. T., Goelela. V.S., Verschuren. L., Toet. K., vanDuyvenvoorde. W., Stroeve. J.H., Cnubben. N. (2013) Differential effects of drug interventions and dietary lifestyle in developing type 2 diabetes and complications // A systems biology analysis in ldlr−/− mice. PLoS ONE. – P.8.

24 Dovgolis S.A., Fomina I.G., Ulybysheva M.A. et al. (2007) Issledovaniye sutochnyy dinamiki razlichnykh proyavleniy narusheniya ritma serdtsa u bol'nykh IBS s mertsatel'noy i khronicheskoy serdechnoy nedostatochnost'yu FK II-III NYHA [Study of the diurnal dynamics of various manifestations of cardiac arrhythmias in IHD patients with atrial fibrillation and chronic heart failure FC II-III NYHA] Health and education in the 21st century. Concepts of diseases of civilization: materials of the International Congress. Moscow, P. 725-727.

25 Karp V.P., Dovgolis S.A., Fomina I.G., Ulybysheva M.A. (2007) Issledovaniye sutochnoy dinamiki razlichnykh proyavleniy narusheniya ritma serdtsa u bol'nykh s mertsatel'noy aritmiyey i khronicheskoy serdechnoy nedostachnost'yu [Study of the daily dynamics of various manifestations of heart rhythm disturbances in patients with atrial fibrillation and chronic heart failure] Materials of the 4th scientific-practical conference "New technologies in recreation of public health". Vladikavkaz, pp. 75-78.

26 Pisaruk A.V., Shatilo V.B., Lishnevskaya V.Yu. (2005) Sutochnyye kolebaniya variabel'nosti ritma serdtsa pri starenii Daily variations in heart rate variability during aging. Institute of Gerontology, Academy of Medical Sciences of Ukraine, Kiev, P. 9-11.