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Multidimensional Phase-Space Analysis in Assessing the Health of Patients with Hypertensive Disease in the North of Russia

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Abstract

The purpose of the research was to assess the health of patients with hypertensive disease (HTD) before and after combined rehabilitation treatment, and to identify the features of chaotic pattern of various body-system parameters in the course of treatment. In the study, patients with uncomplicated HTD underwent a combined medical rehabilitation treatment based on leech reflex therapy; we assessed the degree of activity of the autonomic nervous and cardiorespiratory systems, systolic blood pressure (SBP) and diastolic blood pressure (DBP), and coagulation and lipid profiles of each patient before and after the treatment. Data and bioinformatic analysis of the vector of HTD patients' condition showed a multifactorial rise in sanogenetic potential and adaptability of patients after the treatment. It was found that after a course of combined rehabilitation treatment, the pathology quasi-attractor parameters have moved to sanogenesis (health) quasi-attractor.

Keywords

Hypertension disease; Leech reflex therapy; Phase spaces; Quasi-attractor (QA); Sanogenesis

Introduction

In the Russian Federation, cardiovascular diseases rank second after respiratory diseases in medical aid appeal ability (12.2%), fourth in morbidity with temporary disability (9.4%), and first in persistent disability, causing about half of all cases of primary disability retirement—47.9%.

About 180,000 patients with circulatory diseases were registered in KhMAD—Ugra in 2013. Every year about 30,000 new cases are registered; about 4,500 people die of heart and vascular diseases and as many become disabled. Over the last 5 years, the mortality rate from circulatory diseases has ranged from 285.9 to 301.6 per 100,000 people in KhMAD. The people with elevated blood pressure prevail among the appeals for medical aid. Over 2013 the proportion of these diseases in KhMAD was 5.3 per 1,000 people (indicator calculated on the adult population of 18 and older) [1].

Hypertensive disease (HTD) is one of the most important medical problems. The main danger of high blood pressure is that it leads to the rapid development or progression of atherosclerotic process, coronary heart disease (CHD), stroke, heart failure, and renal disease. In 70% of cases, HTD causes strokes. The risk of a stroke is directly proportional to an increase in arterial blood pressure (ABP). The risk of a stroke increases with a small increase in ABP. In part, this fact explains the tougher specification of normal ABP levels in all international and national guidelines for diagnosis and treatment of HTD. The weakest link in the functioning of oxygen supply system in hypertensive patients is the activity of "arterial vascular bed providing a total peripheral resistance." Individuals living in the north and especially hypertensive patients were diagnosed to have a set of symptoms, which indirectly indicates a more pronounced effect on the sympathetic nervous system, and which, in combination with the increased metabolic rate and intense heart function, contributes to the short-term but severe morbidity of HTD in the north. Apparently, reactivity in higher vegetative centers in hypertensive patients changes, causing increased sensitivity of patients to the northern ecosystem's environment changes.

For a long time, the recommendations for HTD treatment considered ABP values alone as the only and main parameter that defines the need and type of therapy. To date, the concept of HTD prevention and treatment provides an assessment of total cardiovascular risk. The simultaneous elevated blood pressure and other risk factors can reinforce each other, and together they provide a higher cardiovascular risk than the sum of its individual components. There is evidence that it is more difficult to control blood pressure in patients from high-risk group, and they often need, in addition to the prevailing antihypertensive medication, the prescription of lipid-lowering, antiplatelet therapy necessary to impact the overall cardiovascular risk that steadily leads to unwanted polypharmacy and side effects [2]. To date, there are no clear criteria for the choice and practical application of medical rehabilitation methods for treating such a widespread disease as HTD justified by evidence-based medicine, and there are no scientifically based criteria for the effectiveness of nondrug HTD therapies, which indicates the obvious need for further research in this area.

The program of HTD combined treatment suggested by us includes small doses of medicines, leech therapy, phytotherapy (constantly conducted phytotherapy leads to the process stabilization and prevents the development of organic changes of cardiovascular system for a long time), and oxygen therapy, improving oxygenation and microcirculation, which is one of the basic ways of disease treatment. The pronounced positive effect of leech therapy in the HTD treatment and its impact on the reduction of total cardiovascular risk is due to the biologically active substances (BAS) secreted by leeches. Leech saliva containing BAS provides anticoagulative, hypotensive, anti-ischemic, antisclerotic,

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sedative action, protective antithrombotic, energy, acoustic, negentropic, aqua structuring effects. It also eliminates the microcirculatory disturbances. Drug-free treatment of HTD helps reduce blood pressure; it reduces the need for antihypertensive drugs and increases their efficacy, allows for correction of risk factors, and assists in primary and secondary HTD prevention in patients with elevated blood pressure who have risk factors and/or target lesions [3,4].

Materials and Methods

The objects of this study were patients with hypertension disease receiving combined rehabilitation treatment. We treated HTD patients with the following drugs: ACE inhibitor renipril (drug substance—enalapril maleate) in a daily dose of 5-10 mg, depending on the level of blood pressure, and patients with tachycardia (heart rate [HR] more than 90 beats per minute) were treated with beta blocker (concor 2.5 mg). For some patients drug therapy was canceled. In addition to drugs, we used the rehabilitation treatment methods—leech therapy (method of affecting the reflex, biologically active points, tender zones [head]). Up to 120 specimens were used for a course of treatment. In addition, for treating patients with more acute symptoms, we used herbal medicine (to allay nervous and mental tension and stabilize the vasomotor center, we used medicinal plants in threshold individual doses with sedative properties: valerian, motherwort, lime, lemon balm, mint, peony, meadowsweet), oxygen therapy with New Life oxygen concentrators, and the equipment of the American Air Ser company (the enrichment of the inhaled air with oxygen improves the alveolar–arterial oxygen difference, increases the delivery of oxygen to the tissues, and eliminates and reduces tissue hypoxia).

We studied 72 people, 36 male and 36 female, suffering from HTD. The patients were divided into groups by 18, those who had lived for less and for more than 5 years in the north. The average age of patients was 40.0 ± 15.0; the average stay in the north of the studied patients was 30.0 ± 15.0. Patients with concomitant somatic diseases, secondary hypertension, and other diseases of the cardiovascular system were excluded from the survey. All surveyed patients gave informed voluntary consent to perform diagnostic tests, treatments, and physiotherapy. We used a pulse oxymeter device "Eloks"—01S2 (CJSC EMC "NoviePribori," Samara) to evaluate the activity of patients' autonomic nervous system by heart rate variability (HRV). We assessed HR; beats per second—a HR calculated in the average-value interpulse intervals in the analyzed sample; SYM—an activity index of the sympathetic part of the autonomic nervous system; PAR (relative value unit [rvu])—an activity index of the parasympathetic autonomic nervous system; INB (rvu)—tension index characterizing the centralization degree of regulatory influences on the HR; HF (high frequency wave power in the range from 0.4 to 0.15 Hz); mc2—reflects the activity of the macromyelon parasympathetic cardio inhibitory center; LF (low frequency wave power in the range from 0.15 to 0.04 Hz); mc2—reflects the activity of the macromyelon sympathetic centers, which determines cardiac stimulant and vasoconstrictive effects; VLF (very low frequency wave power in the range from 0.04 to 0.0033 Hz)—reflects the activity of the central ergotropic and humoral-metabolic mechanisms of HR regulation; TP (total power spectrum); and mc2—reflects the total effect on HR of all regulation levels. In addition, the patients' hematological parameters were assessed: prothrombin index (PTI), F (fibrinogen), APTT (activated partial thrombo-plastin time), total cholesterol (TC), LDL (low-density lipoprotein), HDL (high-density lipoprotein), TG (triglycerides), and Hgb (blood hemoglobin level).

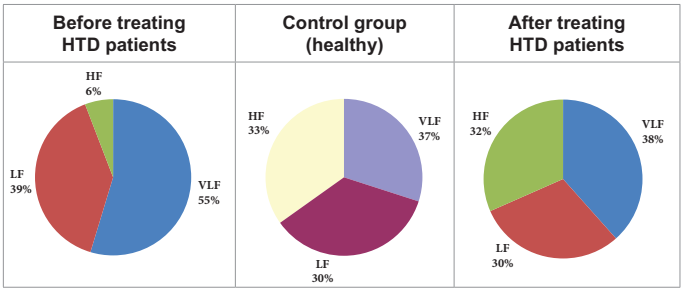

Table 1

Gender	HTD patient treatment (n = 36)	General asymmetry value rX (rvu)	General V value Vx (rvu)
Women	Before treatment	64.36	15.79×10^{29}
	After treatment	2.79	76.44×10^{19}
	Control	2.80	77.20×10^{19}
Men	Before treatment	55.89	33.18×10^{22}
	After treatment	1.77	71.76×10^{22}
	Control	1.85	72.05×10^{22}

Table 2: QA-parameter identification of the integral-time characteristics of HTD patients before and after the treatment

Gender	HTD patient treatment (n = 36)	General asymmetry value rX (rvu)	General V value Vx (rvu)
Women	Before treatment	2,265.40	2.61×10^{23}
	After treatment	631.22	7.78×10^{21}
	Control	632.00	7.91×10^{21}
Men	Before treatment	4,655.89	8.57×10^{23}
	After treatment	625.75	2.42×10^{21}
	Control	631.00	2.15×10^{21}

Table 3: QA-parameter identification of the spectral characteristics of HTD patients before and after the treatment

Hemostatic profile (Quick's thrombin time, F, APTT) was determined by coagulometric technique using SYSMEX CA 50 analyzer, the SIMENS test (Japan). Lipid profile (TC, LDL, HDL, triglycerides) was determined by fermentative-colorimetric technique using Cobas 6000 analyzer, the Roche Diagnostics test (Switzerland). The hemoglobin indicator was investigated automatically by the photometric method, owing to the transformation to SLS-Hb, using sodium lauryl sulfate.

The obtained data were processed by the variation statistics method up to the confidence interval using the STATISTICA 6, IBM PC BIO-STAT software package as described by S. Glantz. Normal data distribution was assessed by calculating using the Shapiro-Wilk test. It was found that not all the parameters were described by the normal distribution law, so further dependency calculations were made by nonparametric statistics methods using the Wilcoxon test. Besides, the obtained data were processed using the original program: "Identification of the parameters of the vector behavior quasi-attractors of biosystems state in the multidimensional phase space," "The program of medical diagnostics based on the distance between the actual point of the human body state vector and the nearest centers of quasi-attractors" [3,5].

Gender	HTD patient treatment (n = 36)	General asymmetry value rX (rvu)	General V value Vx (rvu)
Women	Before treatment	4.23	331.34×10^{19}
	After treatment	2.54	46.54×10^{19}
	Control	2.60	45.88×10^{19}
Men	Before treatment	5.19	218.16×10^{19}
	After treatment	3.04	265.89×10^{16}
	Control	3.01	263.76×10^{16}

Table 4: Identification of hematological indices of HTD patients before and after the treatment

	Women before treatment	Women after treatment	Men before treatment	Men after treatment
Women before treatment	0.00	112.74	53.70	113.95
Women after treatment	**112.74**	0.00	165.41	1.48
Men before treatment	53.70	165.41	0.00	166.61
Men after treatment	113.95	1.49	**166.61**	0.00

Notes: **112.74**—distance between the centers of stochastic QA in women before and after the treatment (112.74×10^{16} rvu); **166.61**—distance between the centers of stochastic QA in men before and after the treatment (166.61×10^{16} rvu).

Table 5: Distance matrix (z_{ij}) between the stochastic behavior centers of the vector of HTD patients' body condition before and after the treatment

	Women before treatment	Women after treatment	Men before treatment	Men after treatment
Women before treatment	0.00	174.41	44.71	176.39
Women after treatment	**174.41**	0.00	218.43	2.00
Men before treatment	44.71	218.43	0.00	220.41
Men after treatment	176.39	2.00	**220.41**	0.00

Notes: **174.41**—distance between the centers of chaotic QA in women before and after the treatment (174.41×10^{16} rvu); **220.41—**distance between the centers of chaotic QA in men before and after the treatment (220.41×10^{16} rvu).

Table 6: Distance matrix (z_{ij}) between the chaotic behavior centers of the vector of HTD patients' body condition before and after the treatment

Results and Discussion

When comparing the integral-temporal and spectral characteristics before and after the treatment by using the Wilcoxon test, the reliable significant changes of all parameters in all groups were marked (SYM, PAR, INB, HR, VLF, LF, HF, TOTAL) ($p < 0.05$), except for SpO2 parameter. The oxygen saturation reliably significantly changed only in the group of men who had lived in the north for less than 5 years ($p \leq 0.049$), indicating that this category of persons has the greatest sensitivity to oxygen therapy carried out together with leech reflex therapy, and it is associated with improved rheological blood properties and tissue hypoxia reduction. The SpO2 changes in other groups are statistically insignificant.

According to the results of statistical processing of the SBP, DBP, and coagulation and lipid profiles before and after rehabilitation treatment by using the Wilcoxon test, the parameter changes of the following groups are insignificant: (1) TC and TG in women living for less than 5 years in the north ($p \leq 0.163$ and $p \leq 0.796$, respectively); and (2) HDL in men living for more than 5 years in the north ($p \leq 0.182$). This is due to the initially normal values of these parameters included in the interval of reference, and after treatment they remained within those limits without significant dynamics. The parameters prevailing majority is significantly different at the critical significance level of $p \leq 0.05$ before and after the treatment, which indicates a significant positive effect of combined rehabilitation treatment based on leech reflex therapy [6,7].

When comparing the spectral characteristic charts before and after the rehabilitation treatment and those of the control (healthy person) groups, a pronounced decrease in the activity of ergotropic and humoral-metabolic mechanisms of HR regulation (VLF from 55 to 38%), a decrease in the activity of the sympathetic centers of the macromyelon (LF from 39 to 30%), and an increase in the activity of the parasympathetic centers of the macromyelon (HF from 6 to 32%) are observed, which indicate the predominance of the total score of parasympathetic (cardioinhibitory) and sympathetic (cardiac stimulant) centers of the macromyelon over the central mechanisms of HR regulation.

The after-treatment indicators and those of the control group are most relevant to each other, which confirms an increase in adaptive capacity and transition of human body state vector to the most gentlest mode of function. Also, hematological parameters, SBP, and DBP normalized in the course of the treatment, which proves the sanogenetic effect of the combined method of HTD rehabilitation treatment applied by us.

Thus, after a combined rehabilitation treatment, we observed a decrease in the general asymmetry and the total volume of a parallelepiped in all groups of patients, regardless of gender differences, which indicates a favorable trend of human body state-vector behavior, an increase in adaptive capacities, and a significant tendency in QA pathology to self-organization and the transition to QA sanogenesis (recovery). The increase in adaptive capacity is of particular importance in the extreme conditions of living in the north of Russia [4,6–9].

Computation of attractor-to-attractor distance matrix (z_{ij}) between the centers of stochastic quasi-attractors showed that after the treatment, there was a reduction of distances between statistical mathematical expectations. This dynamics is interpreted by us as a quantitative mapping of the high efficacy of the therapeutic modality and control [7–10].

The combined use of bioinformatic analysis and statistical data processing program helped to confirm the possibility of a combined rehabilitation treatment not only for stabilizing the blood pressure but also for the homeostasis harmonious regulating [5–7,10].

Conclusion

Within the scope of the bioinformatic analysis, the method of multidimensional phase spaces has allowed us to show the features of the autonomic nervous and cardiorespiratory systems' functioning, the features of coagulation indices, and lipid metabolism in hypertensive patients, and allowed us to evaluate the efficacy of the combined rehabilitation treatment, which is based on nonpharmacological methods of influence [8–10].

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