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DYNAMIC CHANGES IN SPECTRAL HEART RATE VARIABILITY PARAMETERS IN PACED BREATHING TEST IN PATIENT WITH UNCONTROLLED ARTERIAL HYPERTENSION AND POLYMORBIDITY

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A clinical case of a patient with uncontrolled hypertension and polymorbidity. The paced breathing test was made, was found prevalence of low frequency influences at the initial stage and its intensification at the resting stage, growth of the total power of heart rate variability spectrum (TP) with respiratory modulation. The course of the disease worsened the appearance of new-onset atrial fibrillation (registered paroxysm on Holter monitoring); the general deterioration of the patient's state reflected HRV changes on sinus rhythm tracing - significantly reduced TP growth in response to paced breathing, an increase in LF/HF (ratio of low frequency to high frequency waves), as well as switching to the neurohormonal level of heart rate regulation at the resting stage. After the treatment the growth of TP in response to the test has increased and LF/HF level has decreased.

KEY WORDS: arterial hypertension, heart rate variability, paced breathing

ДИНАМІЧНІ ЗМІНИ ПАРАМЕТРІВ ВАРІАБЕЛЬНОСТІ СЕРЦЕВОГО РИТМУ У ПРОБІ З МЕТРОНОМІЗОВАНИМ ДИХАННЯМ У ПАЦІЄНТА З НЕКОНТРОЛЬОВАНОЮ ГІПЕРТЕНЗІЄЮ І ПОЛІМОРБІДНІСТЮ

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Описано клінічний випадок пацієнта з неконтрольованою артеріальною гіпертензією та поліморбідністю. Проведена проба з метрономізованим диханням, виявлено превалювання низькохвильових впливів на етапі фонового запису і посилення їх на етапі відпочинку, приріст загальної потужності спектру варіабельності серцевого ритму (ТР) при модуляції дихання. Перебіг захворювання погіршила поява вперше виявленої фібриляції передсердь (зарєстрований пароксизм при холтерівському моніторингуванні), загальне погіршення стану пацієнта відбили зміни ВСП при запису з синусовим ритмом - значне зниження приросту ТР у відповідь на метрономізоване дихання, підвищення LF/HF (відношення хвиль низької частоти до височастотним), а також перемикаання регуляції серцевого ритму на стадії відпочинку на нейрогормональний рівень. Після проведеної терапії збільшився приріст ТР у відповідь на пробу, знизився рівень LF/HF.

КЛЮЧОВІ СЛОВА: артеріальна гіпертензія, варіабельність серцевого ритму, метрономізоване дихання

ДИНАМИЧЕСКИЕ ИЗМЕНЕНИЯ ПАРАМЕТРОВ ВАРИАБЕЛЬНОСТИ СЕРДЕЧНОГО РИТМА В ПРОБЕ С МЕТРОНОМИЗИРОВАННЫМ ДЫХАНИЕМ У ПАЦИЕНТА С НЕКОНТРОЛИРУЕМОЙ ГИПЕРТЕНЗИЕЙ И ПОЛИМОРБИДНОСТЬЮ

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Описан клинический случай пациента с неконтролируемой артериальной гипертензией и полиморбидностью. Проведена проба с метрономизированным дыханием, выявлено превалирование низкочастотных влияний на этапе фоновой записи и усиление их на этапе отдыха, прирост общей мощности спектра вариабельности сердечного ритма (ТР) при модуляции дыхания. Течение заболевания усугубило появление впервые выявленной фибрилляции предсердий (зарегистрирован пароксизм при холтеровском мониторировании), общее ухудшение состояния пациента отразили изменения ВСП при записи с синусовым ритмом – значительное снижение прироста ТР в ответ на

метрономизированное дыхание, повышение LF/HF (отношение волн низкой частоты к высокочастотным), а также переключение регуляции сердечного ритма на стадии отдыха на нейрогормональный уровень. После проведенной терапии увеличился прирост TP в ответ на пробу, снизился уровень LF/HF.

КЛЮЧЕВЫЕ СЛОВА: артериальная гипертензия, вариабельность сердечного ритма, метрономизированное дыхание

INTRODUCTION

Essential hypertension is one of the most widespread diseases [1–2], dangerous, primarily for its complications [1–3], the risk of which increases significantly especially in the case of uncontrolled hypertension that may be associated with inadequate antihypertensive therapy or with its non-systematic use [3–4]. The presence of comorbidities, that exacerbate hypertension, significantly worsens the prognosis of these patients [5].

Heart rate variability (HRV) is not only noninvasive, but also a convenient method of evaluating the functional state of the cardiovascular system. A test with paced breathing is considered to be one of the most effective components of the HRV evaluation, which gives wide opportunities for the dynamic analysis of the effectiveness of antihypertensive therapy, changes in the autonomous regulation of heart rate, both at rest and during respiratory modulation and provides possibilities for an individual approach to each patient [6–7].

Heart rate variability spectral analysis allows to estimate the ratio of the distribution of the main components of HRV spectrum: high frequency waves (HF), reflecting the sympathetic and in some extent parasympathetic influences; very low frequency waves (VLF) that characterize the neurohormonal regulation of the heart rate, the low frequency waves (LF), responsible for the vagal control of HRV, and LF/HF – ratio of the low frequency waves to high frequency waves. Also important role in HRV analysis plays TP – the total power of heart rate variability spectrum [8].

CASE STUDY

A 53-year old woman presented with complaints on periodically appearing headaches, mostly in occipital area, «feeling of heaviness in the head» provoked by physical overload or stress, palpitations, poorly controlled blood pressure.

Patient also complained on inability to decrease and control her excessive weight.

Patient was first diagnosed with arterial hypertension near 5 years ago; since 2013 she tried to treat herself with occasional intake (once in several weeks) of amiodarone as a «some doctor had advised», but she didn't notice significant improvement of her state. In Jan 2014 she was examined in National Institute of Therapy named by L.T. Malaya, where the diagnosis was made: essential arterial hypertension II grade 2 stage, high risk, the left ventricle hypertrophy, aortic stenosis I st., heart failure IIa st. with preserved systolic function, II functional class, impaired fasting glucose. Bisoprolol 5 mg per day, enalapril 10 mg per day was prescribed. The patient took prescribed medications occasionally, non-systematically.

The patient has been working as a cook at the market during last 10 years. She denies smoking, drug abuse, drinks alcohol occasionally; denies chronic cardiovascular diseases and acute cardiovascular events (including sudden cardiac death) in close relatives. Had no operations, traumas in the past; in 2014 was diagnosed with single-nodular goiter, subclinical hypothyroidism.

On objective examination: The general status of the patient is satisfactory, clear consciousness, posture is active. Height is 162 cm, weight – 120 kg, BMI = 45 kg/m². Skin: pale-pink, with preserved moistness and elasticity; visual mucous membranes are pink, moist, undamaged; fat tissue is developed excessively, distributed symmetrically. Peripheral edemas are absent. Thyroid gland: by palpation both lobes of thyroid gland are diffusely enlarged, painless; there is a mass near 1cm in diameter in the right lobe. Lungs: resonance percussion sound, vesicular breathing over the lungs fields, RR 19 pm. Heart borders are extended to the left on 1 cm, heart activity is rhythmic with HR 72 bpm. Heart tones are rhythmic, with mid-systolic ejection murmur of moderate intensity in the II and V points of auscultation.

Blood pressure *sin* 144/100 mm Hg, *dext* 146/102 mm Hg, radial pulse is synchronous, rhythmic at 72 bpm.

Abdomen: abdominal girth – 133,5 cm, abdomen is painless on superficial and deep palpation in all regions. Liver at the costal margin, painless; spleen is not palpable. Absence of vascular sounds during abdomen auscultation. Pasternatskiy sign is negative on both sides. Urination is free, painless.

The results of current patient's investigations were: clinical full blood count, urinalysis, creatinine, urea, blood electrolytes, ALT, AST, within the normal range; fasting plasma glucose FPG – 6,5 mmol/l (N – 3,3–5,5 mmol/l); lipid profile – very low density lipoprotein cholesterol VLDL-C-1,52 mmol/l (N – < 1,05 mmol/l), low density lipoprotein cholesterol LDL – C (N – < 2,59 mmol/l) – 5,1 mmol/l, high density lipoprotein cholesterol HDL-C – 1,4 mmol/l (N – 1, 04–1,55 mmol/l), triglycerides – 3,35 mmol/l (N – < 2,3 mmol/l), total cholesterol – 8,2 mmol/l (N – < 5,2 mmol/l), atherogenic coefficient – 4,85 U (N – < 3U).

ECG: sinus rhythm, heart rate – 71/min, complete right bundle branch block; echocardiography – increased stiffness of aorta and leaflets of aortic valve with their fibrotic changes, signs of moderate aortic stenosis (opening restricted to 1,2 cm, pressure gradient on aortic valve – 20 mm Hg), left ventricle hypertrophy, diastolic dysfunction of left ventricle, EF – 63 %.

HRV paced breathing test – showed imbalance of autonomous nervous system with prevalent very low frequency and decreased high frequency components of HRV spectrum, low TP in the initial stage; paced breathing showed positive growth of TP and parasympathetic response with increased high frequency involvement, resting stage demonstrated non-significant growth of TP in comparison with initial stage and intensification of low frequency influences (see table).

Diagnosis: essential hypertension stage II, grade 2, high risk. Left ventricular hypertrophy. Atherosclerosis of the aorta and its valve with aortic stenosis 2 st. Heart failure IIA with preserved ejection fraction, II functional class. Obesity grade 3. Dyslipidemia. Impaired fasting plasma glucose. Single-nodular goiter 1st stage with unspecified function.

Prescriptions of the patient were: life style modifications, lisinopril 5 mg per day, atorvastatin 20 mg per day, aspirin – 75 mg daily. After 2 weeks of therapy the general status of the patient has been improved, her blood pressure was running on values 130–132/85–90. Next visit was recommended after 3 month but the patient didn't come.

After 8 month the patient came with complaints on periodically appearing (once or twice in a month) attacks of extreme weakness, palpitations, dizziness and burning chest pain with irradiation into the interscapulum space; such episodes developed usually «without any obvious reasons»; relieved by prolonged rest and intake of corvalol. Several times attacks were so severe that patient fainted.

Patient first started to notice such attacks for about 4 months ago; first they were rare and insignificant but then their intensity and frequency began to increase. Near 5 months ago she stopped antihypertensive therapy by herself but the last week she began to take lisinopril 5 mg per day again.

On objective examination – there are edemas of the lower thirds of sheens; blood pressure *sin* 160/100 mm Hg, *dext* 164/106 mm Hg, other physical signs without significant changes.

On laboratory and instrumental investigations: lipid profile – VLDL – 1,2 mmol/l, LDL – 5,1 mmol/l, HDL – 1,3 mmol/l, triglycerides – 2,27 mmol/l, total cholesterol – 7,26 mmol/l, atherogenic coefficient – 4,84 U; FPG – 5,0 mmol/l; ultrasonography of thyroid gland: diffuse changes of thyroid gland with enlargement of both lobes of thyroid gland; there are nodules in both lobes; thyroid function test: free thyroxin FT4 – 0,993 ng/dl (N – 0,93–1,7 ng/dl), free triiodothyronine FT3 – 3,02 pg/dl (N – 2,0–4,4 pg/dl), serum thyrotropin TSH – 1,45 µIU/mL (N – 0,27–4,2 µIU/mL), thyroid peroxidase antibodies TPO – 16,13 IU/mL (N – < 34,0 IU/mL). Echocardiography – signs of atherosclerosis, moderate aortic stenosis (pressure gradient on aortic valve – 30 mm Hg), moderate dilation of the left atrium, concentric hypertrophy of left ventricle, diastolic dysfunction of left ventricle, EF – 61 %.

Holter monitoring – 20.10.2015 reported episode of atrial fibrillation with ventricular rate 90–160, lasting 54 minutes, during which

observed following complaints – weakness, burning sensation behind the sternum and interscapulum region, the feeling of impending syncope. Also during the period of observation were registered 7 supraventricular extrasystoles.

HRV paced breathing test (PBT) sinus rhythm tracing – characterized by decreased heart functional state with extremely low TP, prevalence of low frequency components of HRV spectrum with significantly increased LF/HF ratio and high level of very low frequency waves; the reaction on paced breathing was positive with increased parasympathetic activity, although TP showed poor growth; in resting stage occurred intensification of neurohormonal impact on heart rate regulation (see table).

Diagnosis: essential hypertension stage II, grade 2, high risk. First diagnosed atrial fibrillation, tachy form (20.10.2015 registered episode of atrial fibrillation with duration of 54 minutes). Left ventricular hypertrophy. Atherosclerosis of the aorta and its valve with aortic stenosis 2 st. Heart failure IIA with preserved ejection fraction, II FC. Obesity grade 3. Dyslipidemia. Nodular goiter 1st stage. Euthyrosis.

Prescriptions for the patient were: sotalol 40 mg twice daily with control of ECG QT interval in 3 days, if QT remain normal, dosage should be increased up to 80 mg twice a day with QT interval control in 3 days, furosemide 40 mg a day every 3-rd day, under control of plasma electrolytes balance), lisinopril 5 mg daily, atorvastatin 20 mg once daily, aspirin 100 mg daily.

After 7 months of treatment, the patient's general condition improved significantly, attacks of atrial fibrillation were almost ceased, blood pressure stabilized at the level of 125–130/80–85. On Holter's monitoring episodes of atrial fibrillation were not detected.

Paced breathing test (sinus rhythm tracing) demonstrated sympatonia with increased neurohormonal contribution to the HRV spectrum in initial stage, paced breathing stage was characterized with increase of vagal parameters, and in initial stage was observed significant shift to neurohormonal influences (see table).

RESULTS AND DISCUSSION

Dynamic changes in spectral parameters of HRV in the patient are shown in table.

Table

Dynamic changes of the HRV spectral components in paced breathing test (sinus rhythm tracings)

Spectral HRV parameters	06.02.15, 1 st visit	13.10.15, 2 nd visit	13.06.16, 3 rd visit
Initial stage			
VLF, %	52	43	40
LF, %	32	46	46
HF, %	16	11	14
LF/HF	2,09	4,01	3,25
TP, ms ²	254	142	239
Paced breathing			
VLF, %	33	23	37
LF, %	13	31	20
HF, %	54	46	43
LF/HF	0,23	0,68	0,47
TP, ms ²	1819	264	861
Resting stage			
VLF, %	49	69	63
LF, %	43	27	30
HF, %	9	4	7
LF/HF	4,84	7,23	4,44
TP, ms ²	351	189	580

Note: VLF - very low frequency waves, LF - low frequency waves, HF – high frequency waves, LF/HF - ratio of the low-frequency waves to high-frequency waves, TP – total power of HRV spectrum.

Dynamic changes in spectral indices quite clearly reflected the functional state of the heart rhythm regulation, depending on the

course of the disease. Changes of LF/HF ratio showed increase in low frequency influences on the 2nd visit, compared with the 1st one,

which were especially pronounced in the resting stage, where LF/HF reached the value of 7, 23. The deterioration of vagal response to paced breathing on the 2nd visit compared with 1st one was also apparent. However on the 3rd visit, was noted decline in the LF/HF ratio at all stages of the breathing test, thus

demonstrating the improvement of the patient's condition in connection with the effectiveness of the therapy and systematic intake of drugs.

Dynamic changes in LF / HF index are illustrated in Figure 1.

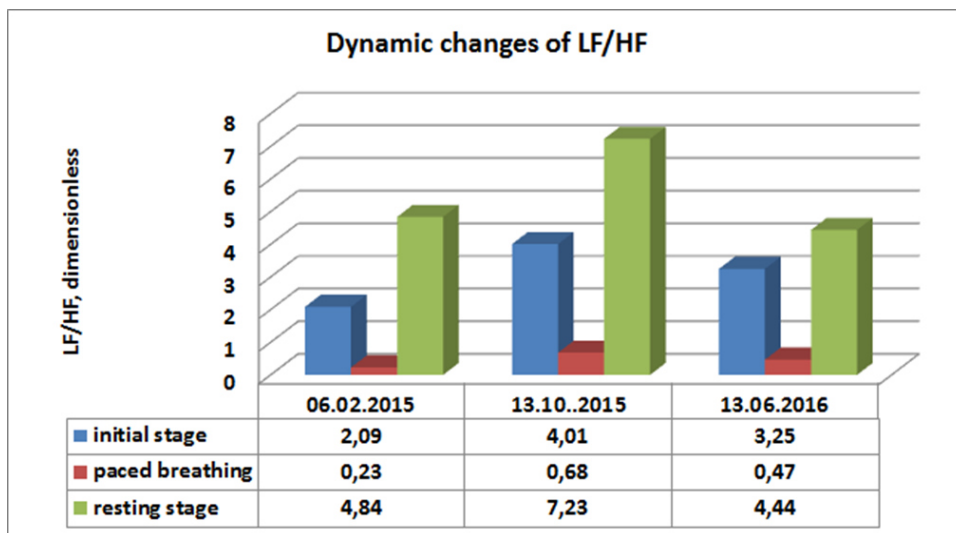


Fig. 1. Dynamic changes of index LF / HF in paced breathing test.

Dynamic changes in the total power TP showed lower values of this parameter at the initial stage of the paced breathing test at all visits, but on the 1st visit a marked TP growth was noted as response to paced breathing, while in the 2nd visit increase of TP was very insignificant, illustrating reduced functionality of heart rate regulation in connection

with the deterioration of the patient's condition. The 3rd visit showed improvement of TP growth in response to respiratory modulation in comparison with the 2nd visit, as well as a more pronounced increase of this index in resting stage.

Dynamic changes in the total power spectrum TP are reflected in the Figure 2.

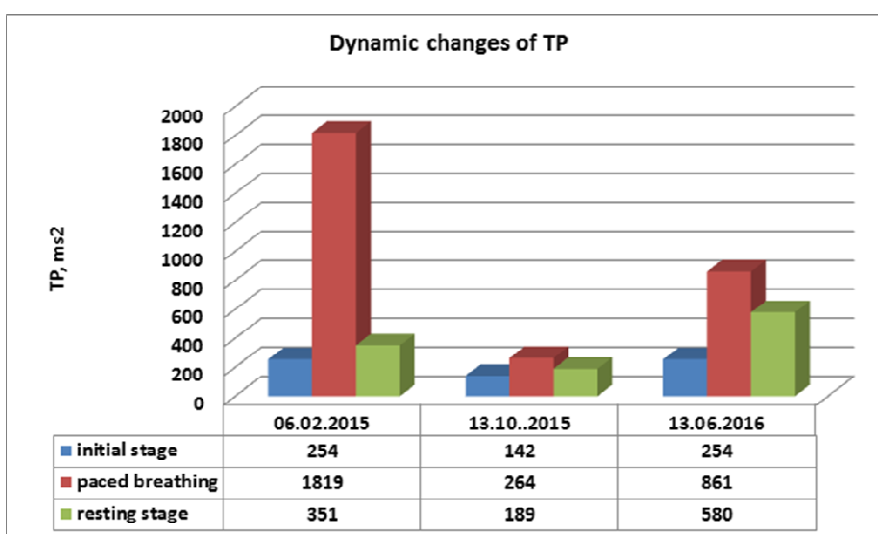


Fig. 2. Dynamic changes in the total power spectrum TP in paced breathing test.

Influence of neurohormonal HRV components in the initial stage was most pronounced on the 1st visit, and prevailed

over low-frequency index in paced breathing stage. In the 2nd and 3rd visit was observed a significant increase in LF component

compared to the VLF, but at the resting stage was noted a shift towards to increase in neurohormonal effects, by means of reducing low-frequency and high-frequency waves.

Thus the deterioration of the patient's condition that manifested with the registered episode of atrial fibrillation due to uncontrolled hypertension, non-systematic approach to drug intake and due to existing concomitant diseases was reflected by the aggravation of imbalance of the heart rate regulation related to the reduced regulatory capacity of the autonomous nervous system characterized by the decrease of the total

power of the HRV spectrum and intensification of sympathetic and especially neurohormonal influences. On the other hand, after effective application of therapeutic regimens reverse changes in the spectral parameters of HRV occurred.

CONCLUSIONS

Assessment of heart rate variability by means of paced breathing test is a useful tool for dynamic monitoring of the patient's condition that allows to improve evaluation of treatment efficacy and to individualize therapy.

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