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Clinical researches

UDC: 612.062

THE DEPENDENCE OF SPECTRAL CHARACTERISTICS OF HEART RATE VARIABILITY FROM BODY MASS INDEX IN CONDITIONALLY HEALTHY

Alumuku M., Okonjo C., Hazem O., Belal S. A. S.
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In 102 conditionally healthy volunteers aged from 19 to 30 years (average age is 19,53 ± 11 years) the volatility of heart rate variability (HRV) spectral parameters depending on body mass index (BMI) were evaluated. According to WHO recommendations on the calculation and interpretation of BMI were such groups of volunteers: underweight, normal body weight, overweight, obesity I degree, obesity II degree, obesity III degree. Among HRV parameters were evaluated total power (TP, ms^2), power of very low frequency (VLF, ms^2), low frequency (LF, ms^2) and high frequency (HF, ms^2) domains of HRV spectrum in the 5-minute intervals of ECG in I standard lead. The data were processed by methods of nonparametric statistics. It was established that spectral characteristics of HRV in volunteers with normal BMI have a high TP with harmonious relations between VLF, LF and HF domains; decreased or increased BMI provokes TP reduction by decreasing power of all domains of HRV (VLF, LF, HF) with a predominance of VLF proportion and this effect increases with the degree of deviation of the parameter.

KEY WORDS: heart rate variability, body mass index, conditionally healthy volunteers

ЗАЛЕЖНІСТЬ СПЕКТРАЛЬНИХ ХАРАКТЕРИСТИК ВАРІАБЕЛЬНОСТІ СЕРЦЕВОГО РИТМУ ВІД ІНДЕКСА МАСИ ТІЛА У УМОВНО ЗДОРОВИХ ДОБРОВОЛЬЦІВ

Алумуку М., Оконджо К., Хазем О., Бєлал С. А. С.
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У 102 умовно здорових добровольців у віці від 19 до 30 років (середній вік 19,53 ± 11 років) була оцінена мінливість спектральних параметрів варіабельності серцевого ритму (ВСР) в залежності від індексу маси тіла (ІМТ). Відповідно до рекомендацій ВОЗ щодо розрахунку та інтерпретації ІМТ були виділені такі групи добровольців: недостатня вага, нормальна вага, надмірна вага, ожиріння I ступеня, ожиріння II ступеня, ожиріння III ступеня. Серед показників ВСР оцінювали загальну потужність (ТР, ms^2), потужність дуже низьких (VLF, ms^2), низьких частот (LF, ms^2) і високих (HF, ms^2) частот доменів спектру ВСР в 5-хвилинних інтервалах ЕКГ в I стандартному відведенні. Дані були оброблені методами непараметричної статистики. Встановлено, що спектральні характеристики варіабельності серцевого ритму у добровольців з нормальним ІМТ мають високу ТР із гармонійним співвідношенням між доменами VLF, LF, HF; зниження або підвищення ІМТ провокує зниження ТР за рахунок зменшення потужності всіх спектрів ВСР (VLF, LF, HF) з переважанням долі VLF і цей ефект зростає зі збільшенням ступеня відхилення параметра.

КЛЮЧОВІ СЛОВА: варіабельність серцевого ритму, індекс маси тіла, умовно здорові добровольці

ЗАВИСИМОСТЬ СПЕКТРАЛЬНЫЕ ХАРАКТЕРИСТИК ВАРИАБЕЛЬНОСТИ СЕРДЕЧНОГО РИТМА ОТ ИНДЕКСА МАССЫ ТЕЛА У УСЛОВНО ЗДОРОВЫХ ДОБРОВОЛЬЦЕВ

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У 102 условно здоровых добровольцев в возрасте от 19 до 30 лет (средний возраст 19,53 ± 11 лет) была оценена изменчивость спектральных параметров вариабельности сердечного ритма (ВСР) в зависимости от индекса массы тела (ИМТ). В соответствии с рекомендациями ВОЗ по расчету и интерпретации ИМТ были выделены следующие группы добровольцев: недостаточный вес, нормальный вес, избыточный вес, ожирение I степени, ожирение II степени, ожирение III степени.

Среди показателей ВСР оценивали общую мощность (TP, ms2), мощность очень низких (VLF, ms2), низких частот (LF, ms2) и высоких (HF, ms2) частот доменов спектра ВСР в 5-минутных интервалах ЭКГ в I стандартном отведении. Данные были обработаны методами непараметрической статистики. Установлено, что спектральные характеристики вариабельности сердечного ритма у добровольцев с нормальным ИМТ имеют высокую TP с гармоничным соотношением между доменами VLF, LF, HF; снижение или повышение ИМТ провоцирует снижение TP за счет уменьшения мощности всех спектров ВСР (VLF, LF, HF) с преобладанием доли VLF и этот эффект возрастает с увеличением степени отклонения параметра.

КЛЮЧЕВЫЕ СЛОВА: вариабельность сердечного ритма, индекс массы тела, условно здоровые добровольцы

INTRODUCTION

Body mass index (BMI) is one of the most important physiological characteristics of the body and reflects matching of the weight of the person to its growth [1]. The use of this parameter in clinical practice will help to establish the deficit, excess body weight and obesity of varying degree.

Heart rate variability (HRV) is the earliest indicator of violations of adaptation reserves of the body and has important prognostic value for both healthy people and patients with diseases of various organs and systems [2].

Taking into account that the variability of body weight can be considered as a failure of the adaptation to environmental conditions [3], it is interesting to assess the state of human regulatory systems based on spectral characteristics of HRV in conditionally healthy volunteers with different BMI.

The study was performed as part of KhNU scientific research «Development and research of system of automatic control of heart rate variability», № registration 0109U000622.

OBJECTIVE

Purpose of the study is to explore the dependence of spectral characteristics of heart rate variability from body mass index in conditionally healthy volunteers.

MATERIALS AND METHODS

The study involved 43 volunteers aged from 19 to 30 years (average age is 24,5 ± 5,0 years). Inclusion criteria: age over 20 years, absence of acute and chronic diseases, absence of pernicious habits.

BMI was assessed on the basis of the formula BMI = m/h, where m – the weight in kilograms, h – growth in meters [1]. According to WHO guidelines for BMI interpretations [1] were such groups of volunteers: underweight, normal body weight, overweight, obesity I degree, obesity II degree, obesity III degree (table).

Table

Characteristic of groups of volunteers

Groups of volunteers	BMI (kg/m^2)	Number of volunteers (n)	Average age (M ± sd)
Underweight	16 – 18,5	20	22,7 ± 3,2
Normal weight	18,5 – 25	25	22,5 ± 2,9
Overweight	25 – 30	20	23,5 ± 6,2
Obesity I degree	30 – 35	15	24,1 ± 4,1
Obesity II degree	35 – 40	17	28,1 ± 10,0
Obesity III degree	more than 40	5	26 ± 3,6

Note: $p < 0,01$ between groups

Among HRV parameters were evaluated total power (TP, ms2), power of very low frequency (VLF, ms2), low frequency (LF, ms2) and high frequency (HF, ms2) domains of HRV spectrum in the 5-minute intervals of ECG in I standard lead [2] on the diagnostic complex «Cardiolab 2009».

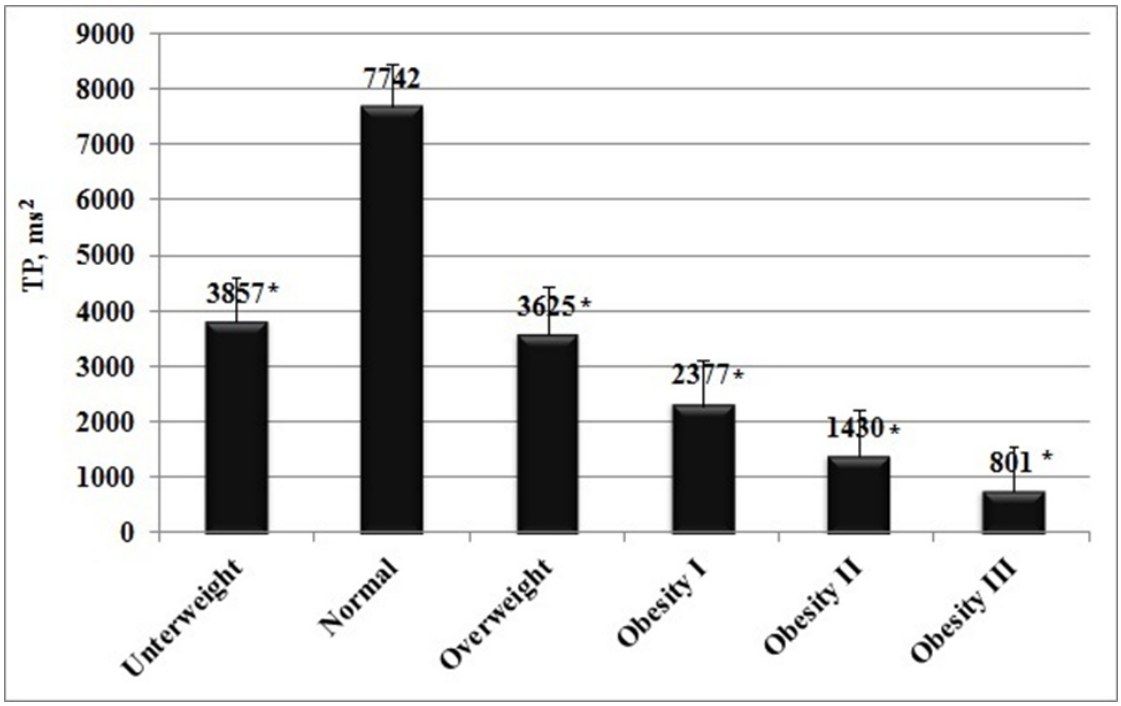
Statistical analysis of the results for each subject was carried out using Microsoft Excel. Average values (M) and standard deviations

(sd) of TP, VLF, LF and HF of all records of all subjects were put down in spreadsheet. The differences reliability of each parameter between groups of volunteers was determined by Mann-Whitney U-test [4].

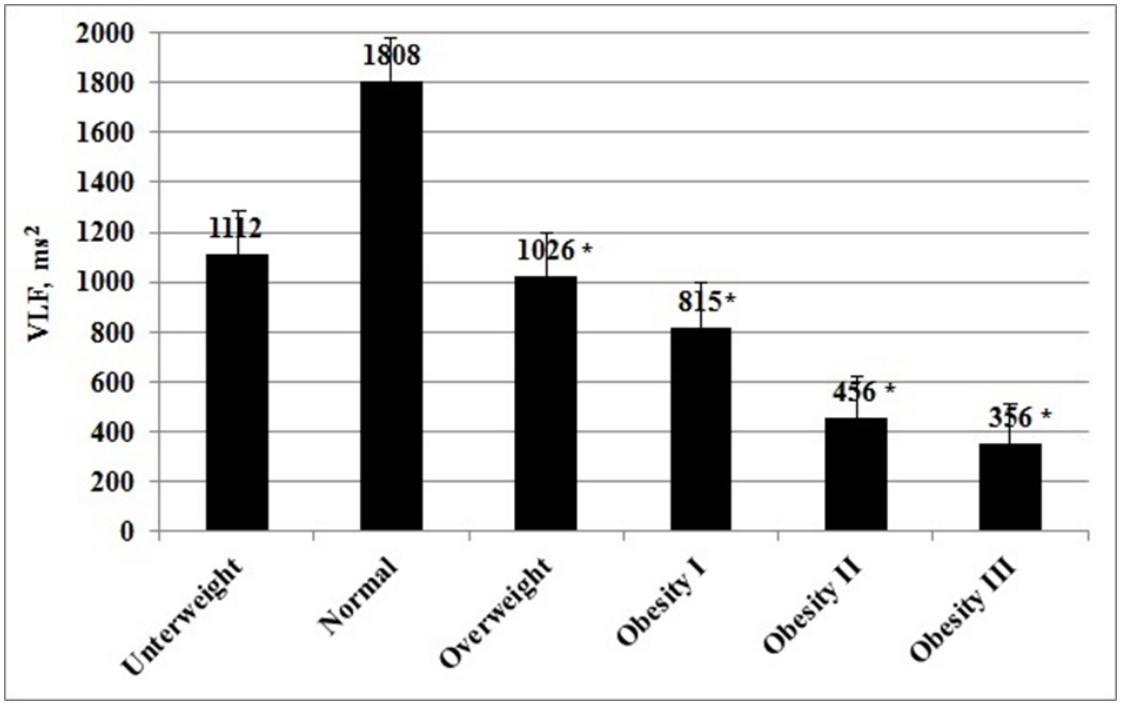
RESULTS AND DISCUSSION

Average values (M) and standard deviations (sd) of TP, VLF, LF and HF in all groups of volunteers presented in figure. Spectral characteristics of HRV in patients with normal BMI have a high TP with harmonious relations between VLF, LF and HF domains. All BMI abnormalities provoke TP reduction by decreasing power of all domains of HRV (VLF, LF, HF) and this effect increases with the degree of deviation.

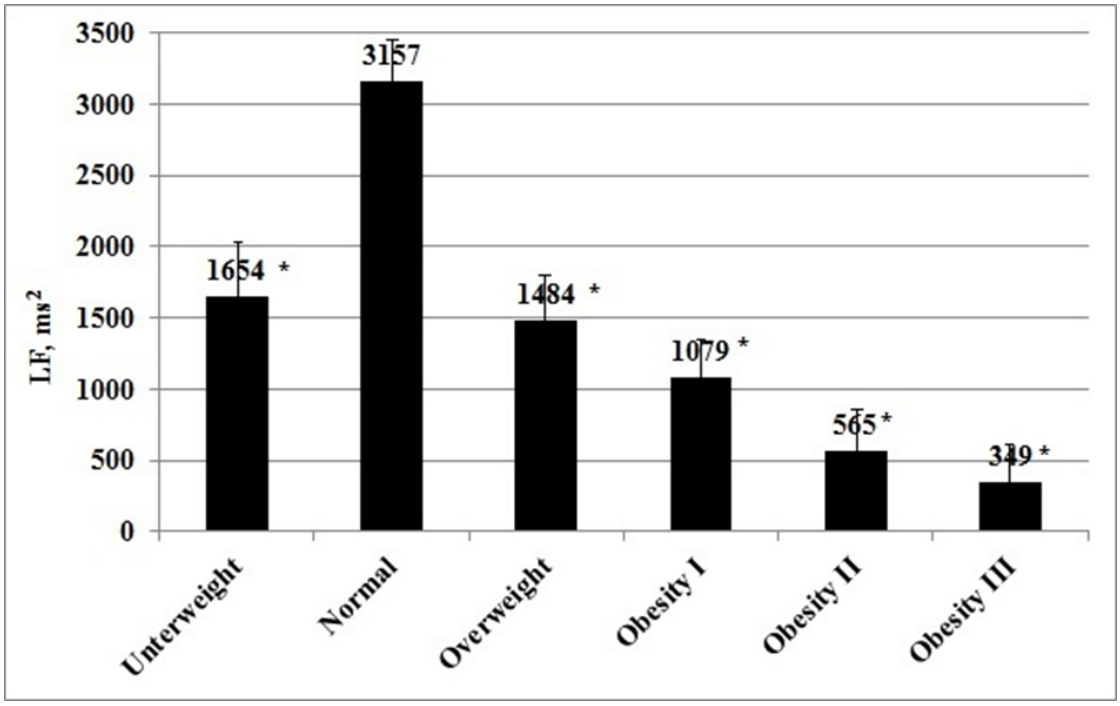
a)



b)



c)



d)

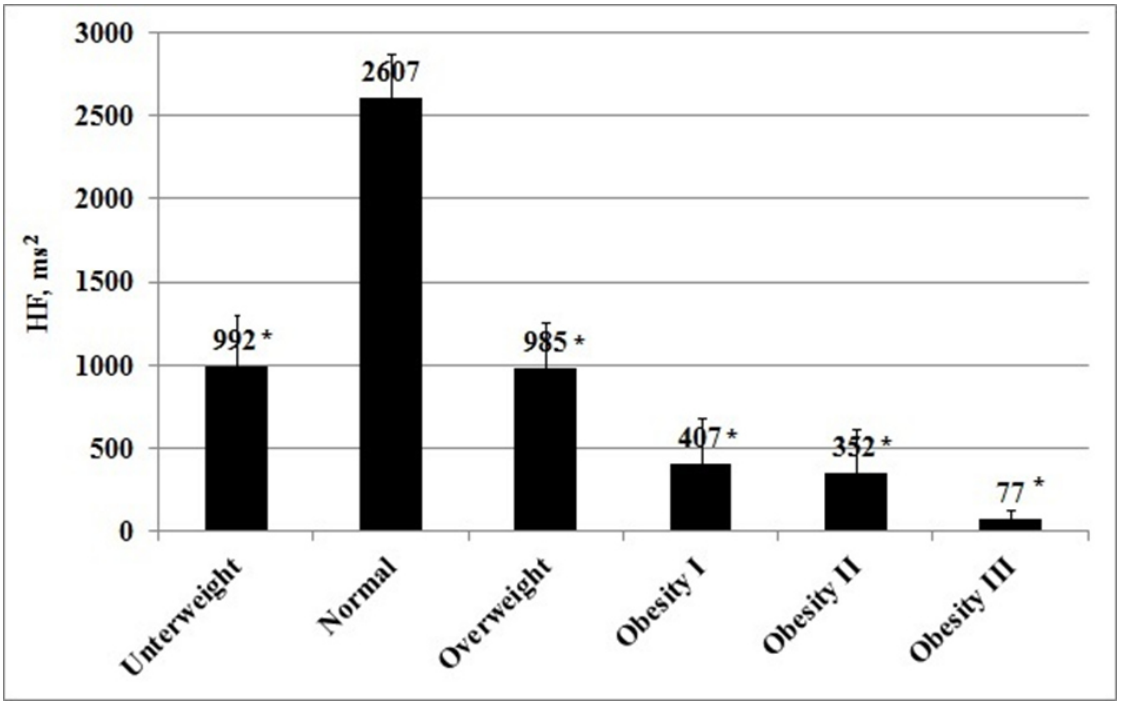


Fig. Average values (M) and standard deviations (sd) of TP (a), VLF (b), LF (c) and HF (d) in volunteers with underweight, normal body weight, overweight, obesity I degree, obesity II degree, obesity III degree.

Notes: $p < 0,01$ against volunteers with normal body weight.

Several studies [5–7] have shown that the lack or excess weight can be seen as a failure of adaptive reserves of the human body; however, there are no accurate data on the specific changes in the autonomic regulation in the literature, which makes our investigation topical.

Among the non-invasive assessment of the state of the regulatory systems techniques heart rate variability (HRV) is the most informative

and widely used in clinical practice [2]. BMI is a versatile and most convenient means of evaluating body weight, which allowed identifying underweight, normal body weight, overweight, obesity I degree, obesity II degree, obesity III degree [1].

We have found that spectral characteristics of HRV in patients with normal BMI have a high TP (7742 ms^2) with harmonious relations between VLF (23 %), LF (43 %) and HF (34 %) domains. In volunteers with unter- and overweight was observed practically same reduction of TP (3857 and 3625 ms^2 against 7742 ms^2 in volunteers with normal BMI) by all domains (VLF, LF, HF), but with preservation of their proportions. In volunteers with obesity was observed increases with the degree reduction of TP by declining power of all domains of HRV (VLF, LF, HF) with a predominance of VLF proportion.

CONCLUSIONS

1. Spectral characteristics of HRV in patients with normal BMI have a high TP with harmonious relations between VLF, LF and HF domains.
2. Decreased or increased BMI provokes TP reduction by declining power of all domains of HRV (VLF, LF, HF) with a predominance of VLF proportion.
3. TP reduction with declining power of all domains of HRV (VLF, LF, HF) with a predominance of VLF proportion increases with the degree of deviation of BMI.

PROSPECTS FOR FUTURE STUDIES

It is interesting to evaluate the volatility of spectral parameters of HRV in conditionally healthy volunteers with normalizing of BMI by dietary recommendations.

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ASSESSMENT OF CHANGES IN THE DISTRIBUTION RATIOS OF ULTRA-LOW-FREQUENCY, LOW-FREQUENCY AND HIGH-FREQUENCY COMPONENTS OF HEART RATE VARIABILITY DURING THE PACED BREATHING TEST IN PATIENTS WITH ARTERIAL HYPERTENSION

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Were studied the distribution ratios of ultra-low-frequency, low-frequency and high-frequency components of the heart rate variability (HRV) as an indicator of the state of humoral and autonomic sympathetic and parasympathetic elements in regulation of heart rate in 35 patients with arterial hypertension (AH) aged 59 ± 5 years in the paced breathing test. Evaluation of spectral parameters of HRV was performed with the help of hardware and software «Kardiolab» («HAI-Medica»). Patients were divided into 3 groups according to the degree of power reduction of low-frequency and high-frequency waves of HRV during the transition from spontaneous breathing to paced one: 1st group- less than 5 times; 2nd group – 5–20 times; 3rd group – more than 20 times. Statistical analysis was performed by means of parametric and nonparametric methods using Microsoft Excel 7.0. It was found that in patients with hypertension was observed prevalence of humoral effects in comparison with the sympathetic and parasympathetic parameters. The greater was the contribution of humoral component to the HRV spectrum, the lower was the response of HRV to the respiratory modulation.

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

ОЦІНКА ЗМІНИ РОЗПОДІЛУ СПІВВІДНОШЕНЬ УЛЬТРАНИЗЬКОЧАСТОТНИХ, НИЗЬКОЧАСТОТНИХ І ВИСОКОЧАСТОТНИХ КОМПОНЕНТІВ ВАРІАБЕЛЬНОСТІ СЕРЦЕВОГО РИТМУ У ПАЦІЄНТІВ З АРТЕРІАЛЬНОЮ ГІПЕРТЕНЗІЄЮ В ПРОБІ З МЕТРОНОМІЗОВАННИМ ДИХАННЯМ

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Було вивчено розподіл співвідношень ультранизькочастотних, низькочастотних і високочастотних компонентів варіабельності (ВСР) як показників стану гуморальної і вегетативної симпатичних і парасимпатичних ланок регуляції серцевого ритму у 35 пацієнтів з артеріальною гіпертензією (АГ) у віці 59 ± 5 років у пробі з метрономізованним диханням. Оцінка спектральних параметрів ВСР проводилася за допомогою програмно-апаратного комплексу «Кардіолаб» («ХАІ-Медика»). Пацієнти були розділені на 3 групи за ступенями зниження відношень потужностей низькочастотних і високочастотних хвиль ВСР при переході зі спонтанного на метрономізованне дихання: 1 група – менш ніж в 5 разів; 2 група – в 5–20 разів; 3 група – більш ніж в 20 разів. Статистична обробка даних проводилася параметричними і непараметричних методами з використанням Microsoft Excel 7.0. Було встановлено, що у пацієнтів з АГ спостерігається переважання гуморальних впливів над симпатичними і парасимпатичними. Чим більше виражений внесок у ВСР гуморальної складової спектру, тим нижче реакція показників ВСР на модуляцію дихання.

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

ОЦЕНКА ИЗМЕНЕНИЯ РАСПРЕДЕЛЕНИЯ СООТНОШЕНИЙ УЛЬТРАНИЗКОЧАСТОТНЫХ, НИЗКОЧАСТОТНЫХ И ВЫСОКОЧАСТОТНЫХ КОМПОНЕНТОВ ВАРИАБЕЛЬНОСТИ СЕРДЕЧНОГО РИТМА У ПАЦИЕНТОВ С АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИЕЙ В ПРОБЕ С МЕТРОНОМИЗИРОВАННЫМ ДЫХАНИЕМ

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Изучено распределение соотношений ультранизкочастотных, низкочастотных и высокочастотных компонентов вариабельности сердечного ритма (ВСР) как показателей состояния гуморального и вегетативных симпатического и парасимпатического звеньев регуляции сердечного ритма у 35 пациентов с артериальной гипертензией (АГ) в возрасте 59 ± 5 лет в пробе с метрономизированным дыханием. Оценка спектральных параметров ВСР проводилась с помощью программно-аппаратного комплекса «Кардиолаб» («ХАИ-Медика»). Пациенты были разделены на 3 группы по степеням снижения отношения мощностей низкочастотных и высокочастотных волн ВСР при переходе со спонтанного на метрономизированное дыхание: 1 группа – менее чем в 5 раз; 2 группа – в 5–20 раз; 3 группа – более чем в 20 раз. Статистическая обработка данных проводилась параметрическими и непараметрическими методами с использованием Microsoft Excel 7.0. Установлено, что у пациентов с АГ наблюдается преобладание гуморальных влияний над симпатическими и парасимпатическими. Чем больше выражен вклад в ВСР гуморальной составляющей спектра, тем ниже реакция показателей ВСР на модуляцию дыхания.

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

INTRODUCTION

One of the important pathogenetic links of hypertension is a violation of the autonomic balance with a predominance of sympathetic and humoral effects, reduced activity of parasympathetic components of autonomous nervous system [1–2]. These changes are making a tangible contribution to the severity of the disease and may complicate the selection of antihypertensive therapy that frequently is empirical. The use of heart rate variability techniques (HRV) is a valuable addition to the standard set of diagnostic procedures in modern medicine that makes possible not only to assess the severity of pathological changes in the autonomic regulation [3–5], and take them into account in the prescription of antihypertensive drugs, as well as dynamically control the functional state of the cardiovascular system during patient treatment [6–7].

Spectral analysis of HRV allows evaluate the frequency characteristics of the components of the spectrum and their distribution in influencing the modulation of heart rate, which is particularly important when examining patients with arterial hypertension.

Spectral indices of heart rate HF, LF, VLF are defined as high, low and ultra-low-frequency components of HRV spectrum, and reflect the sympathetic, parasympathetic and suprasegmentally influences in the regulation of heart rate. HF is characteristic for vagal control of autonomic modulation of heart rate, LF – to sympathetic and, to a certain extent, the parasympathetic components of HRV, VLF contributes to humoral component of HRV spectrum [8].

A paced breathing test allows determine the state of autonomous regulation and first of all the level of vagal response at controlled respiration [9], and the level of return to its initial state in the final stage of test [10]. Therefore, researches in this field are not only of theoretical but also of practical interest and allow determine the pathogenetic links of hypertension in each individual patient, and thus provide opportunities for more effective and targeted therapy in these patients.

OBJECTIVE

The purpose of this article is to determine the changes in the ratios of distribution of ultra-low-frequency, low-frequency and high-frequency components in patients with essential arterial hypertension in the paced breathing test.

MATERIALS AND METHODS

A total of 35 hypertensive patients aged 40 to 70 years (mean age – 59 ± 5 years).

Inclusion criteria were: hypertension I-III degree, stage I-III with stable angina of FC I–III, chronic heart failure FC I–III I–IIA stage.

Exclusion criteria were: acute myocardial infarction, unstable angina, chronic heart failure IV FC, valvular heart disease, implanted pacemakers, endocrinological diseases (diabetes, thyroid disease, etc.), exacerbation of systemic diseases.

Clinical diagnosis of essential arterial hypertension was determined in accordance with the recommendations of the Ukrainian Association of Cardiology [11].

Blood pressure measurement was carried out by the method of Korotkov using the tonometer Microlife BP AG1-20.

The study of HRV was performed using the «CardioLab» («HAI-Medica») computer software containing the algorithm for determining the HRV parameters.

The test with the modulated (paced) breathing with double (visual and sound) metronome was performed in the supine position of patients, at the same time and consisted of 3 stages. In the first initial resting stage the patients were maintained at rest breathing freely in familiar to them rhythm and depth of breathing for 5 minutes to ensure that a true resting HRV values were obtained; in the second stage of paced breathing patients were instructed to perform breathing in breathing rate of 6 times per minute with additional control of visual and sound metronome for 5 minutes; in the third final resting stage the patients were breathing in a free manner for 5 minutes.

As a result of the test next indices were evaluated: TP (total power of the spectrum), LF (low-frequency waves), VLF (very-low-frequency waves), HF (high-frequency waves), LF/HF (ratio of the low-frequency waves to high-frequency waves).

The test results were interpreted on the basis of international standards (protocols of the European Society of Cardiology) [8].

Depending on the changes of LF/HF ratio between paced breathing stage and the initial stage, reflecting the level of regulatory capacity of the autonomic nervous system, patients were divided into 3 groups: the first group – LF/HF decrease of less than 5 times, second group – reducing the LF/HF in 5–20 times, group 3 – LF/HF decrease of more than 20 times in paced breathing stage compared to the initial one.

In each group clinical and spectral parameters of HRV were compared and evaluated in all 3 stages of the paced breathing test.

The Microsoft Excel 7.0 software was used in statistical processing of obtained data. Parametric statistical data were used. Authenticities of differences between groups were evaluated with non-parametric Mann-Whitney U test. To establish the relationship between quantities parametric variables was used Spearman's correlation analysis. The level of significance was set at $p < 0.05$.

RESULTS AND DISCUSSION

The results of the comparison of the distribution ratio of ultra-low-frequency, low-frequency and high-frequency components in hypertensive patients are shown in fig. 1 and tab. 1.

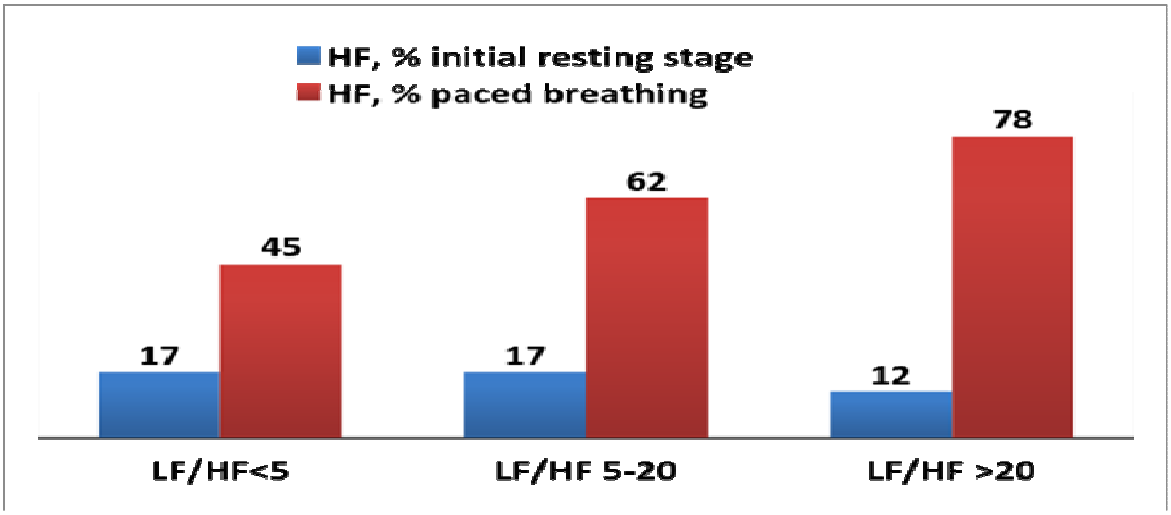

Fig. 1. The extent of HF index growth in the paced breathing stage

Table 1

Spectral HRV parameters depending on the reduction LF/HF in the paced breathing test

Spectral HRV parameters		The degree of reduction of LF/HF in the paced breathing test			Accuracy of differences between the samples, p
		less than 5 times (group 1)	In 5–20 times (group 2)	More than 20 times (group 3)	
TP, ms^2	Initial resting values	1357 ± 2143	787 ± 554	2157 ± 2373	$P_{1-2} > 0,05$ $P_{2-3} < 0.01$ $P_{1-3} > 0,05$
	Paced breathing values	1376 ± 1411	2421 ± 3156	4502 ± 3988	$P_{1-2} > 0,05$ $P_{2-3} < 0.05$ $P_{1-3} < 0.05$
	Final resting values	858 ± 612	825 ± 391	2201 ± 2291	$P_{1-2} > 0,05$ $P_{2-3} < 0.05$ $P_{1-3} > 0,05$
LF, %	Initial resting values	15 ± 3	30 ± 8	36 ± 16	$P_{1-2} < 0,01$ $P_{2-3} > 0,1$ $P_{1-3} < 0.05$
	Paced breathing values	13 ± 8	12 ± 4	7 ± 3	$P_{1-2} > 0,05$ $P_{2-3} < 0.01$ $P_{1-3} < 0.05$
	Final resting values	27 ± 7	30 ± 13	31 ± 17	$P_{1-2} > 0,05$ $P_{2-3} > 0,05$ $P_{1-3} > 0,05$
VLF,%	Initial resting values	67 ± 18	53 ± 15	52 ± 15	$P_{1-2} < 0.05$ $P_{2-3} > 0,05$ $P_{1-3} > 0,05$
	Paced breathing values	42 ± 16	27 ± 14	15 ± 12	$P_{1-2} < 0.05$ $P_{2-3} < 0.01$ $P_{1-3} < 0.01$
	Final resting values	59 ± 11	55 ± 17	59 ± 21	$P_{1-2} > 0,05$ $P_{2-3} > 0,05$ $P_{1-3} > 0,05$
HF, %	Initial resting values	17 ± 16	17 ± 11	12 ± 7	$P_{1-2} > 0,05$ $P_{2-3} > 0,05$ $P_{1-3} > 0,05$
	Paced breathing values	45 ± 20	62 ± 16	78 ± 14	$P_{1-2} > 0,05$ $P_{2-3} < 0.01$ $P_{1-3} < 0.01$
	Final resting values	14 ± 5	15 ± 11	10 ± 6	$P_{1-2} > 0,05$ $P_{2-3} > 0,05$ $P_{1-3} > 0,05$
LF/HF	Initial resting values	1,7 ± 1	2,6 ± 1,8	4,4 ± 4	$P_{1-2} > 0,05$ $P_{2-3} < 0.1$ $P_{1-3} < 0.05$
	Paced breathing values	0,4 ± 0,4	0,4 ± 0,8	0,1 ± 0,07	$P_{1-2} > 0,05$ $P_{2-3} < 0.01$ $P_{1-3} < 0.01$
	Final resting values	2,0 ± 0,5	2,8 ± 2	3,8 ± 1,5	$P_{1-2} > 0,05$ $P_{2-3} < 0.05$ $P_{1-3} < 0,05$

At the initial resting stage an autonomic imbalance with predominance of VLF waves was observed in all 3 groups, indicating the presence of enhanced humoral component of HRV spectrum. The most pronounced prevalence of waves of very low frequency was observed in the first group of patients (VLF = 67 ± 18; $P_{1-2} < 0.05$), whereas in the second and third groups, these values were 53 ± 15 and 52 ± 15, respectively. LF/HF ratio showed fluctuations with increased involvement of low-frequency parameters of

HRV, which was especially pronounced in the third group (LF/HF = 4.4 ± 4, $P_{2-3} < 0.1$, $P_{1-3} < 0.05$). In the 1st group, on the other hand, the share of the low-frequency component of the LF spectrum was less pronounced compared to the 2nd and 3rd groups ($P_{1-2} < 0,01$, $P_{1-3} < 0.05$) and was 15 ± 3. High-frequency indices were approximately at the same level in all groups with no meaningful significant differences between the groups – 16 ± 19, 17 ± 11 and 12 ± 7, respectively in the 1st, 2nd and 3rd groups.

At the stage of paced breathing in third group of patients was noted the most significant involvement of parasympathetic components of HRV spectrum in response to the controlled breathing, high-frequency parameter in this group was observed at the level of – 78 ± 14 ($P_{2-3} < 0.01$, $P_{1-3} < 0.01$). In the same group were observed minimal values of LF compared to the other groups – 7 ± 3 ($P_{2-3} < 0.01$, $P_{1-3} < 0.05$). LF/HF has demonstrated also the same distributions, reflecting vagotonia prevalence in the third group – 0,1 ± 0,07 ($P_{2-3} < 0.01$, $P_{1-3} < 0.01$). The extent of growth in the low-frequency waves of HRV spectrum was different in all 3 groups, and was as follows: in the first group – 28, in the second group – 45 % in the third group – 66 %, thus demonstrating the unequal levels of autonomous regulatory capacity in the examined groups.

Fluctuations of VLF waves also showed different degrees of decline in suprasegmentally influences at paced breathing: in the third group of patients such changes were less pronounced - very low frequency level value decreased by 37 % compared to the initial resting stage and was recorded at 15 ± 12; while in the 1st and 2nd groups, this value fell by only 23 % and 26 %, respectively, and appeared to be 42 ± 16 and 27 ± 14, with significant difference between the groups $P_{1-2} < 0.05$, $P_{2-3} < 0.01$, $P_{1-3} < 0.01$ (fig. 2).

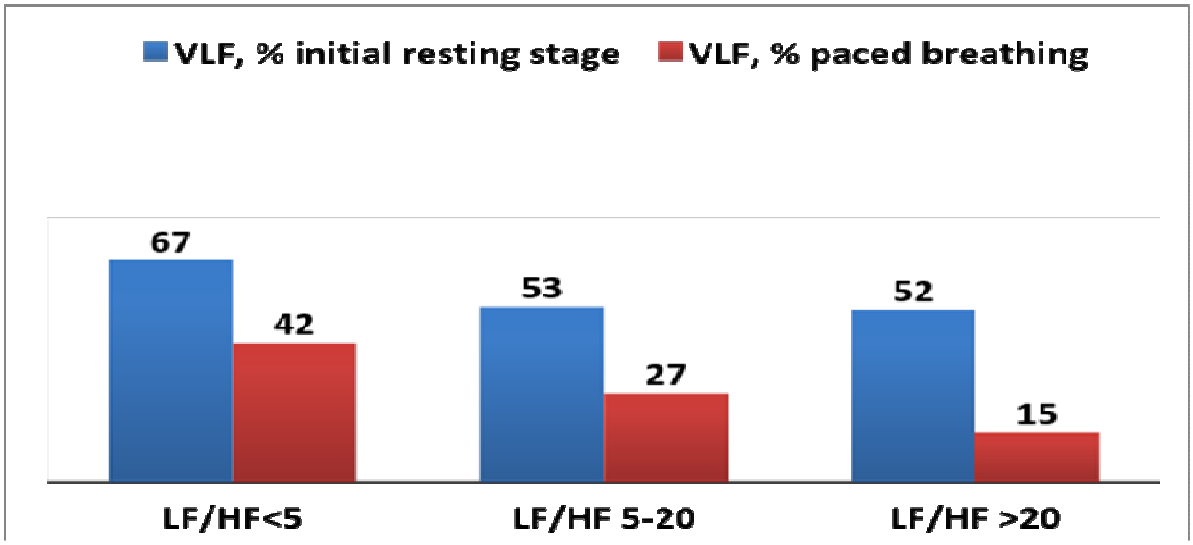

Figure 2. The degree of reduction VLF index in paced breathing stage

Correlations between changes of distribution of VLF and HF waves in paced breathing stage compared with the initial resting stage are shown in tab. 2.

Table 2

Correlations between changes of distribution of VLF and HF waves in paced breathing stage compared with the initial resting stage

	Initial stage-paced breathing Group 1	Initial stage-paced breathing Group 2	Initial stage-paced breathing Group 3
Correlations between increase of HF, ms^2 and decrease of VLF, ms^2	$r_s = -1$; $p < 0.001$;	$r_s = -0.074$; $p > 0.05$;	$r_s = 0.297$; $p > 0.05$;

where r_s – Spearman's rank correlation coefficient, p – p-value

In the final resting stage there were detected slight decrease in the proportion of high-frequency waves of HF in all groups of patients(13 ± 5 – in the 1st group, 15 ± 11 – in the 2nd, 10 ± 6 in the third group of patients); At the same time, the humoral involvement was enhanced, demonstrating increase in VLF waves from 2 % to 7 %, compared with the initial resting stage and was recorded at level of 60 ± 12, 55 ± 17, 59 ± 21 in the 1st, 2nd and 3rd groups respectively. Low-frequency parameter of HRV in the third group in the final resting stage of the breathing test has decreased in comparison with the initial resting stage by 5 % to 31 ± 17; in the 2nd group LF values showed no differences from the same values in initial resting stage (30 ± 13), while in the 1st group, the low-frequency component of HRV spectrum has increased by 11 % to 27 ± 8.

Changes in the total power of the spectrum are shown in fig. 3 demonstrating a lack of growth in TP in response to the paced breathing in the 1st group, while in the second and third groups of patients this parameter had a positive growth during the phase of controlled breathing. In the final resting stage, a decrease of the total power of the spectrum compared to initial values in the 1st group was established; in the 2nd and 3rd groups the value of TP returned back to the initial level.

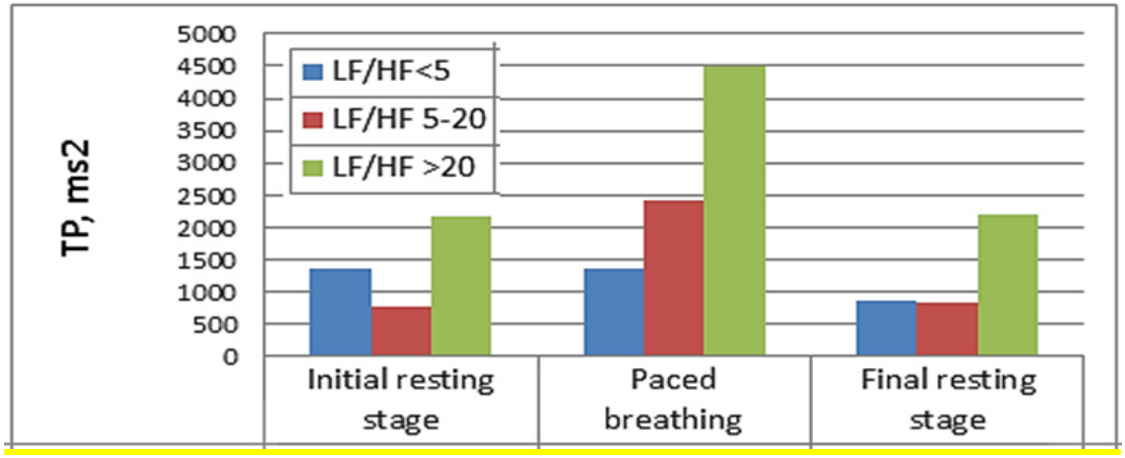

Fig. 3. Changes in the value of total power TP during all stages of the paced breathing test in three groups of patients

Data, according to which in the initial resting stage in all groups of patients a significant rise and even prevalence of humoral effects were shown, while the ratio of LF/HF demonstrated shift towards sympathicotonia, confirms [1, 3, 12–14].

Dysregulation of the autonomous nervous system has been less pronounced in patients with higher levels of vegetative regulation, in which the HRV response to paced breathing with a predominance of vagal component was more significant; also there was the significant increase in the total power TP and a marked reduction in humoral influences. In turn, in patients where the regulatory possibilities of the autonomous nervous system were reduced was observed sufficiently high level of HRV suprasegmentally spectral components not only in the resting (initial) state, but in the stage of paced breathing; the extent of HF wave growth in this group with controlled breathing was very small, also there was found a negative correlation between the degree of increase of HF waves and reduce the level of VLF waves at this stage of the test.

At the final resting stage in patients of all groups remained disturbed state of relations between the components of HRV spectrum, more pronounced in patients with a lower level of autonomous regulation. The degree of inhibition of vegetative response to the groups correlated with excessive activation of humoral mechanisms of heart rate regulation.

Increased humoral effects along with the weakening of autonomous control of heart rate may exacerbate hypertension, thereby

adversely affecting the prognosis of the disease, as evidenced by the study [1, 7, 14].

In accordance with these data defined violations in the relations between the spectral parameters of HRV can be a useful tool for the detection of pathogenetic components of arterial hypertension, which can be used for more accurate and careful selection of antihypertensive drugs [6], and also to stratify the risk of complications in hypertensive patients.

CONCLUSIONS

In patients with arterial hypertension there is a decrease of the total power of the HRV spectrum with a predominance of humoral effects in comparison with sympathetic and parasympathetic influences. Intensity of these changes depends on the autonomous control of heart rate regulation: in patients with reduced regulatory capacity of the autonomous nervous system there is a significant prevalence of suprasegmentally regulatory mechanisms that is characterized not only by disrupted static, but also dynamic balance of HRV.

Reduced possibility of regulation of heart rate can also negatively affect the change in the total power of HRV spectrum in all stages of the paced breathing test; in patients with a decreased level of autonomous regulation there is a lack of TP growth in response to controlled breathing, as well as paradoxical decrease in total power parameter during the final resting stage of the test. These changes contribute negatively in a course of arterial hypertension and are the poor prognostic factor for its outcome.

PROSPECTS FOR FUTURE STUDIES

Considering the fact that the vagal imbalance especially along with the excessive humoral involvement has a significant share in the pathogenesis and clinical picture of arterial hypertension thus influencing on the outcomes of the disease the further investigation of this topic has not only theoretical but also practical value.

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CLINICAL AND INSTRUMENTAL CHARACTERISTICS OF JUVENILE CHRONIC ARTHRITIS EVOLUTION

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The purpose of the study was to investigate the clinical symptoms and evolution of juvenile chronic arthritis (JCA) at different stages of it development. 39 children with duration of JCA from 6 months to 5 years in age from 2 to 18 years were examined. All patients underwent clinical examination, indicators of acute phase of inflammation (CRP, sialic acid, seromucoid, glycoproteins), rheumatoid factor, circulating immune complexes, complement, instrumental methods (X-ray and ultrasound, capillaroscopy of nail bed) were evaluated. Activity of the disease was estimated by disease activity score (DAS28). Statistically was determined the relative value (P). It was found that the disease started with monoarthritis (63,37 %). In the future, in half of the patients was formed oligoarthritis with damaging of large and medium-sized joints (68,25 %). In the majority of surveyed disease occurred against the backdrop of the minimal activity of the inflammatory process. On the stages of evolution recurrence of arthritis were observed in one third of children. If duration of the sickness is more than 5 years, it has become less frequent, than in previous years. The absence of clinical and radiographic manifestations of JCA after the abolition of medical treatment within one year, became the basis for the assumption that the disease remission, which was on the third year of the disease 25,93 %, on the fourth – 33,33 %, on the fifth – 36,36 %. The absence of radiographic signs of bone destruction, disability of patients allows interpreting JCA as a positive option of chronic juvenile idiopathic arthritis.

KEY WORDS: juvenile chronic arthritis, juvenile idiopathic arthritis, children

КЛІНІКО-ІНСТРУМЕНТАЛЬНА ХАРАКТЕРИСТИКА ЕВОЛЮЦІЇ ЮВЕНІЛЬНОГО ХРОНІЧНОГО АРТРИТУ

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Метою дослідження було вивчення клінічної симптоматики та еволюції ювенільного хронічного артриту (ЮХА) на різних етапах розвитку. Обстежено 39 дітей з ЮХА тривалістю від 6 місяців до 5 років, віком від 2 до 18 років. У всіх хворих проводили клінічне обстеження, оцінювалися показники гострої фази запалення (СРБ, сіалові кислоти, серомукоїд, глікопротеїди), ревматоїдний фактор, циркулюючи імунні комплекси, комплемент, застосовувалися інструментальні методи (рентгенологічне та ультразвукове дослідження, капіляроскопія нігтьового ложа). Проводилась оцінка активності хвороби disease activity score (DAS28). Статистично визначали відносну величину (Р). Встановлено, що захворювання нерідко починалося з моноартриту (63,37 %). Надалі у половини хворих формувався олігоартрит з пошкодженням великих і середніх суглобів (68,25 %). У більшості обстежених перебіг хвороби був на фоні мінімальної активності запального процесу. На етапах еволюції рецидиви артриту спостерігалися у третини дітей. При тривалості хвороби 5 років вони стали менш частими, ніж у попередні роки. Відсутність клінічних та рентгенологічних проявів ЮХА після відміни медикаментозного лікування протягом одного року стала підставою для трактування клініко-лабораторної ремісії захворювання, яка склала на третьому році хвороби 25,93 %, четвертому – 33,33 %, п'ятому – 36,36 %. Відсутність рентгенологічних ознак деструкції кісток, інвалідизації хворих трактує ЮХА, як певний хронічний позитивний варіант ювенільного ідіопатичного артриту.

КЛЮЧОВІ СЛОВА: ювенільний хронічний артрит, ювенільний ідіопатичний артрит, діти

КЛИНИКО-ИНСТРУМЕНТАЛЬНАЯ ХАРАКТЕРИСТИКА ЭВОЛЮЦИИ ЮВЕНИЛЬНОГО ХРОНИЧЕСКОГО АРТРИТА

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Целью исследования было изучение клинической симптоматики и эволюции ювенильного хронического артрита (ЮХА) на разных этапах развития. Обследовано 39 детей с ЮХА продолжительностью болезни от 6 месяцев до 5 лет, в возрасте от 2 до 18 лет. Всем больным проводили клиническое обследование, оценивали показатели острой фазы воспаления (СРБ, сиаловые кислоты, серомукоид, гликопротеиды), ревматоидный фактор, циркулирующие иммунные комплексы, комплемент, применялись инструментальные методы (рентгенологическое и ультразвуковое исследование, капилляроскопия ногтевого ложа). Проводилась оценка активности болезни disease activity score (DAS28). Статистически определяли относительную величину (Р). Установлено, что заболевание начиналось с моноартрита (63,37 %). В дальнейшем у половины больных формировался олигоартрит с повреждением крупных и средних суставов (68,25 %). У большинства обследованных болезнь протекала на фоне минимальной активности воспалительного процесса. На этапах эволюции рецидивы артрита наблюдались у трети детей. При продолжительности болезни более 5 лет они стали менее частыми, чем в предыдущие годы. Отсутствие клинических и рентгенологических проявлений ЮХА после отмены медикаментозного лечения в течение одного года стала основанием для предположения о ремиссии заболевания, которая составила на третьем году болезни 25,93%, четвертом – 33,33 %, пятом – 36,36 %. Отсутствие рентгенологических признаков деструкции костей, инвалидизации больных позволяет трактовать ЮХА, как некий хронический положительный вариант ювенильного идиопатического артрита.

КЛЮЧЕВЫЕ СЛОВА: ювенильный хронический артрит, ювенильный идиопатический артрит, дети

INTRODUCTION

Juvenile idiopathic arthritis (JIA, a term was introduced in 1997 by EULAR) is a heterogeneous group of diseases that mainly tends to progressive flow and affects the quality of life of a sick child [1–4]. An important feature is their destructive joint damage that determine prognosis [1, 5–6]. There are three clinical variants of JIA debut: systemic, polyarticular and oligoarticular. Among the latest subtypes were detailed persistent (with damaging in less than 5 joints throughout the disease) and common (arthritis develops in more than 4 joints after 6 months of illness), also psoriatic arthritis, arthritis associated with enthesitis, other arthritis [7–9].

In initial stages of JIA different options, clinical symptoms in the further evolution so often characterized by considerable similarity of symptoms, making it difficult not only for diagnose, but also for right treatment [2, 5, 10]. Especially in this respect stands juvenile chronic arthritis (JCA). This term is used since 1977 by EULAR in case when it is impossible to establish a particular nosology, or when it is possible to predict that disease is in the stage of formation [5, 7]. However, JCA is not foreseen in the existing part of JIA terminology.

OBJECTIVE

The purpose of the study is to improving diagnosis and prognosis of JCA based on the examination of the evolution of symptoms and disease in various stages of development.

MATERIALS AND METHODS

In clinic SI «Institute of children and adolescents health care of the NAMSU» 39 children with JCA lasting from 6 months to 5 years and aged from 2 to 18 years were examined. The average age was $9,85 \pm 0,67$ years. Duration of illness was up to one year in 20,51 % of cases, two years – 25,64 %, three years – 30,77 %, four years – 7,69 %, five years – 17,95 %. Among patients with JCA were more females (53,85 %).

Diagnosis was guided by X International Classification, unified clinical protocols of medical care for children with juvenile arthritis No 832 from 22.10.2012 approved by the Ministry of Health of Ukraine, classification of juvenile idiopathic arthritis (ILAR; 1997, 2001). All sick children were examined including clinical, biochemical, immunological,

radiological, ultrasonic methods. Activity of disese was assessment by disease activity score – DAS28, radiographic signs in joints by Steinbrocker scale.

Changes of articular apparatus structures were determined by ultrasound (US) according to developed protocols. All patients were analyzed by acute phase parameters (CRP, sialic acid seromucoid, glycoproteins), rheumatoid factor (RF), circulating immune complexes (CIC) (screening test), complement (by Chudomels in modification of Kondrashova N. I., 1974).

State of microcirculation in children with JCA was determined by capillaroscopy of nail bed. The method was performed in the morning before a meal in ambient temperature near 20–22 °C by capillaroscope M-70A with a magnification in 28 times that allowing to measure the object with an accuracy of 0,05 mm.

All patients during active manifestation of JCA received nonsteroidal anti-inflammatory drugs (diclofenac 2,5–3 mg/kg/day). 34,12 % of patients received glucocorticoids intraarticular. 72,50 % persons appointed by the disease-modifying drugs, including sulfasalazine 30 mg/kg/day.

The study was conducted during the initial investigation of patients in the clinic SI «Institute of children and adolescents health care of the NAMSU» and in the dynamics within five years of the disease.

Statistical analysis of the results was carried out by using the application Statgrafics-5 with the definition of relative value (P) of investigated characteristics.

RESULTS AND DISCUSSION

Debut of articular manifestations in children has been presented mostly by monoarticular lesions (63,37 %). Changes were observed mainly in large and medium-sized joints. The most vulnerable were joints of the lower extremities – knees (60,93 %), significantly lower – shins (9,75 %) and hipbones (9,75 %). Sometimes can be affected radiocarpal joints (7,31 %) and small joints of hands (2,43 %). Twoness of involving joints was observed in 21,93 % of patients. Articular syndrome was characterized by swelling of the joints with deformation (73,12 %), pain during active (39,77 %) and passive movements (43,87 %).

Noteworthy was the presence of morning stiffness in a small proportion of patients (17,06 %), which was mainly short-term. At 4,87 % of patients was diagnosed by regional hypomyotrophy. Mostly, it was manifested in children with a history of illness for more than 15 months. The functional ability of joints suffering mainly on the background of pain. However, even with a steady arthritis limits of movement had little expression and were easily reversible. Given the potentials impact of connective tissue dysplasia to the appearance and evolution of the disease, which has been studied, each patient was determined by signs of hypermobility of joints (GMJ). It was found that it was observed in 30,77 % of children. It was revealed that GMJ prevailed in the age group 6-15 years (73,12 %) and limitation of movement was absent in the presence of GMJ.

According to the assessment of pathological process by DAS28 activity index low activity was diagnosed in 17,06 %, average – in 15,60 % of patients. In remaining patients process wasn't active.

Acute phase indicators including ESR and CRP were mostly normal (82,87 % and 78,00 % respectively), elevated in patients with polyarthritis and olihoartrytom (14,62 % and 19,50 % respectively). Indicators of RF, CIC and complement didn't have deviations from normal.

According to ultrasound investigation signs of synovitis were detected in 78.00 %. Synovitis was determined by the presence of clinical signs of arthritis. In patients with a longer history of pathological process were detected changes of synovial membrane in the form of thickening and proliferation (12,18 % and 14,62 % respectively).

Radiographic changes in the joints at the end of the first year were found in the half of patients. Mainly it was defined as epiphyseal osteoporosis (49,68 %).

In JCA vascular changes (81,32 %) were found in a small number of vessels in the form of tortuosity, uneven caliber, occasionally - as ischemic zones and single aneurysms (14,75 %). Intravascular disorders (58,44 %) were characterized by the rise mainly in venules with slowing of blood flow and fine-grained aggregation of red blood cells. Perivascular background was involved in the pathological process in 24,91 % of cases as a pale color. Microcirculatory disorders were nonstable, they were decreased with elongation of disease duration and remission and then appeared in the exacerbation of the pathological process.

JCA in children is characterized by propensity to recurrence of the pathological process. Signs of re-arthritis in stages of the evolution of the disease remained shorter than in the debut and developed in previously damaged as well as in healthy joints. Relapses of arthritis were observed in one third of children and were more recorded in the second and third years of the disease (42,11 % and 40,74 %). In five year follow-up it has become less frequent than in previous years.

On stages of an evolution of the articular syndrome took place a shift in the ratio of the amount of joint damage (monooligopolyartritis) to oligoarticular defeats. At the end of the observation significant impairment of joint function was not occurred.

Analysis of clinical symptoms and laboratory and instrumental data in the second year of the disease showed that against a background of minimal activity of the inflammatory process in the majority of patients still have been defeat of large and medium-sized joints (68,25 %). Radiological changes at this stage of the disease were detected in 57,89 % of children and manifested as osteoporosis.

In earlier studies of Lebets I. S. was shown that the clinical course of JCA is characterized by low activity of the inflammatory process, monooligoarticular lesions, arthritis of the knees and ankle joints that persists for a long period of time (4 months or more), relapsing of disease without progression of articular syndrome [11]. In article of Salugina S. A. [12] presents clinical and radiological signs of JCA in children, who are in general agreement with our data. Especially it concerns such important features as a low frequency of symmetrical lesions of small joints, muscular atrophy, morning stiffness and the presence of osteoporosis in the majority of patients. We have found that despite the relapses of JCA on the third or fourth year, in third part of patients was presented complete regression of clinical and ultrasound changes in the joints, and in the five-year history in 54,55 % of patients. However, radiological signs of the disease (osteoporosis) were remained respectively in 37,04 % and 18,18 % of patients. The absence of clinical and radiographic manifestations of JCA after the abolition of medical treatment within one year became the basis for the interpretation of disease remission, which was on the third year of the disease 25,93 %, on the fourth – 33,33%, on the fifth – 36,36 %.

CONCLUSIONS

Despite unknown and possibly different triggers that contribute the development of chronic inflammation in the joints, there are certain patterns in the manifestations of JCA (in the structure of JIA). It was established that the disease is characterized by monooligoarticular destruction of large and medium-sized joints, usually knees and shins with moderately pronounced signs of long-term arthritis. In more than 2/3 of children was found recurrent arthritis on the different stages of the evolution of the pathological process, but mostly in the second and third year of the disease often with damaging of previously healthy joints.

However, most children with JCA have favorable prognosis with the development of resistant or less long-term remission with complete regression of the articular syndrome. At a certain similarity between the clinical manifestations with JRA JCA is distinguished by the absence of symmetry defeat of small joints, bursitis, lesions of the eyes, morning stiffness. Radiographic changes in the joints at JCA less serious than in the JRA. This also applies to deviations in immunological parameters in such patients. JCA is a definite positive chronic variant of JRA in the progress and complications.

PROSPECTS FOR FUTURE STUDIES

The study allowed identifying and describing the clinical and paraclinical manifestations of JCA in children. A promising direction is depth studying of metabolic and immunological changes during JCA and identifying relationships between them. Further research in that direction will help to improve approaches to the treatment of patients with this pathology.

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CLINICAL CHARACTERISTICS OF THE TYPES OF DAILY BLOOD PRESSURE PROFILES IN PATIENTS WITH ARTERIAL HYPERTENSION DEPENDING ON THE SELECTED ABPM INDEX

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The frequency characteristics of the clinical signs of arterial hypertension (AH) according to the daily profile type of systolic (SBP), diastolic (DBP) and pulse (PP) blood pressure were studied. The data showed a significant difference in the frequency of occurrence of AH clinical signs, depending on the type of daily profile of SBP, DBP, and PP. It was concluded that in patients with AH determination only SBP daily profile of is not enough, it's necessary to take into account the types of DBP and PP daily profiles also.

KEY WORDS: ambulatory blood pressure monitoring, systolic blood pressure, diastolic blood pressure, pulse pressure, daily blood pressure profile

КЛІНІЧНА ХАРАКТЕРИСТИКА ТИПІВ ДОБОВОГО ПРОФІЛЮ АРТЕРІАЛЬНОГО ТИСКУ У ПАЦІЄНТІВ З ГІПЕРТОНІЧНОЮ ХВОРОБОЮ ЗАЛЕЖНО ВІД ОБРАНОГО ІНДЕКСУ ДМАТ

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Вивчено частотні характеристики клінічних ознак гіпертонічної хвороби (ГХ) залежно від типу добового профілю систолічного (САТ), діастолічного (ДАТ) та пульсового (ПАТ) артеріального тиску. Отримані дані виявили суттєву різницю частот зустрічаємості клінічних ознак ГХ в залежності від типу добового профілю САТ, ДАТ та ПАТ. Зроблено висновок про те, що у пацієнтів з ГХ визначення одного тільки добового профілю САД недостатньо, необхідно враховувати також і типи добового профілю ДАТ і ПАТ.

КЛЮЧОВІ СЛОВА: ambulatory blood pressure monitoring, systolic blood pressure, diastolic blood pressure, pulse pressure, daily blood pressure profile

КЛИНИЧЕСКАЯ ХАРАКТЕРИСТИКА ТИПОВ СУТОЧНОГО ПРОФИЛЯ АРТЕРИАЛЬНОГО ДАВЛЕНИЯ У ПАЦИЕНТОВ С ГИПЕРТОНИЧЕСКОЙ БОЛЕЗНЬЮ В ЗАВИСИМОСТИ ОТ ВЫБРАННОГО ИНДЕКСА СМАД

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Изучены частотные характеристики клинических признаков гипертонической болезни (ГБ) в зависимости от типа суточного профиля систолического (САД), диастолического (ДАД) и пульсового (ПАД) артериального давления. Полученные данные выявили существенное различие частот встречаемости клинических признаков ГБ в зависимости от типа суточного профиля САД, ДАД и ПАД. Сделан вывод о том, что у пациентов с ГБ определения одного только суточного профиля САД недостаточно, необходимо учитывать также и тип суточного профиля ДАД и ПАД.

КЛЮЧЕВЫЕ СЛОВА: суточное мониторирование артериального давления, систолическое артериальное давление, диастолическое артериальное давление, пульсовое давление, суточный профиль артериального давления

INTRODUCTION

Ambulatory blood pressure monitoring (ABPM) is increasingly used in clinical practice for the diagnosis and prognosis of the arterial hypertension (AH) [1]. Circadian fluctuations in blood pressure (BP) estimated by the degree of its night fall – so-called «sleep-time relative BP

decline» [2], which in most cases is determined only for systolic BP (SBP) changes [3, 4], while the changes in diastolic BP (DBP) and, especially, the pulse pressure (PP), is given much less attention. At the same time it was proved that not only the SBP, but DBP and [5] and, moreover, PP [6] are important predictors of outcomes and success of BP control in AH.

We have previously shown that the distribution of occurrence frequency of the daily profile types of SBP, DBP and PP in patients with hypertension is significantly different [7].

OBJECTIVE

To compare occurrence frequency of the AH clinical characteristics depending on the daily profiles of SBP, DBP, and PP in patients with hypertension to clarify their values in AH diagnosis, prognosis and treatment.

MATERIALS AND METHODS

On the clinical base of the Kharkov city outpatient clinic № 24 53 patients with essential hypertension were examined. The study involved 22 men (42 %) and 31 women (58 %). Average age 57 ± 10 years. The average duration of AH 8 ± 6.5 years. Newly diagnosed AH was detected in 6 patients (11 %). AH of stage I was diagnosed in 11 patients (21 %), stage II – in 31 (58 %), stage III – in 11 (21 %). AH of 1 grade was determined in 21 patients (40 %), grade 2–27 (51 %), grade 3–5 (9 %). Heart failure (HF) was diagnosed in the 40 cases (75 %): HF stage I – 31 (58 %), HF stage IIA – in 8 (15 %), HF stage IIB – 1 (2 %), I functional class (FC) of HF was determined in 16 patients (30 %), II FC – 22 (41 %), III FC – 2 (4 %); coronary heart disease (CHD) – 42 cases (79 %): stable angina (I–III FC) – 8 (15 %), postinfarction cardiosclerosis (PICS) – 3 (6 %), focal aterosclerotic cardiosclerosis (ACS) – 33 (62 %). SBP profile of «dipper» type was set in 22 patients (42 %), «nondipper» – in 25 (47 %), «nightpicker» – in 3 (6 %) and «overdipper» in 3 patients (6 %). DBP daily profile of «dipper» type was defined in 17 cases (32 %), «nondipper» – 16 (30 %), according to «nightpicker» – in 2 (4%) and «overdipper» – in 18 cases (34 %). PP profile of «dipper» type was diagnosed in 4 patients (8 %), «nondipper» – in 18 (34 %), «nightpicker» – in 29 (55 %) and «overdipper» – in 2 patients (4 %).

Diagnosis of AH was made according to the recommendations of the Association of Cardiologists of Ukraine (2007), the European Society of Hypertension and the European Society of Cardiology (2013), the Expert Committee of the World Health Organization (WHO) and the International Society of Hypertension (1999), generalized and stated in a Standardized Clinical Protocol of the primary, emergency and secondary (specialized) medical care «Arterial hypertension» (2012) [8].

CHD diagnosis, stage and functional class of HF was made on the basis of Ukrainian Heart Association recommendations on classification, diagnosis and treatment of cardiovascular diseases (2007) [9].

Exclusion criteria were secondary hypertension, hemodynamically significant valvular heart disease, cardiomyopathy of any genesis, heart failure stage III, FC IV by NYHA, any acute condition (infection, trauma, surgery) within the previous 3 months, chronic diseases in stage of decompensation or exacerbation, cancer, as well as any circumstances that hinder the conduction of ABPM.

To determine the daily BP profile the ABPM was performed using a computer system «Kardiosens» (HAI Medica, Ukraine) with the oscillometric method of blood pressure measurement. The monitoring was performed in the conditions of patient normal working day; the cuff was placed at the non-dominant arm using an appropriately sized cuff. According to Ambulatory Blood Pressure Monitoring International Recommendations 2013 [2], blood pressure was measured every 15 minutes during the day and 30 minutes at night. Daytime and night-time periods were defined based on a diary, in which participants were asked to record their activities and sleep times during the monitoring session. Editing ABPM, in accordance Ambulatory Blood Pressure Monitoring International Recommendations [2] if any value outside preset limits (see below) was detected during a recording, that measurement was rejected:

– systolic blood pressure (SBP) > 250 or < 70 mm Hg,

– diastolic blood pressure (DBP) > 150 or < 40 mm Hg,

– pulse pressure (PP) > 150 or < 20 mm Hg,

– heart rate (HR) > 200 or < 20 per minute.

Also ABPM data series were considered invalid for analysis in the following cases:

– absence of ≥ 30 % of the scheduled measurements,

– lack of data for > 2 consecutive hourly intervals,

– if patient maintained an irregular rest-activity schedule during consecutive 24-h periods of monitoring,

– if the nighttime sleep span was < 6 h or > 12 h [2].

To define the daily profile the nocturnal BP dip was quantified as the relative decline in mean BP from awake (daytime) to asleep (night-time) periods, and was calculated for SBP, DBP and PP separately using the following equation: ((mean awake BP – mean asleep BP) / mean awake BP) × 100 %. Depending on the value of this ration the following types of daily BP profile were defined: «dipper» – physiological decrease in BP during the night – sleep-time relative BP decline 10–20 %; «overdipper» – an excessive fall in BP at night, sleep-time relative BP decline > 20 %; «nondipper» – the lack of BP reduction at night, sleep-time relative BP decline < 10 %; «night-peaker» – night-time BP more than during daily activity, sleep-time relative BP decline < 0 [2].

We determined the frequency ratio of the clinical characteristics of AH for each of the types of daily profile, depending on the selected index ABPM, and compared within the groups of SBP, DBP, and PP profiles.

Calculation of ABPM indices was performed using «Kardiosens» program. Data were analyzed with the software «Microsoft Office Excel 2010» and «STATISTICA», with the clinical signs frequency of occurrence assessment in percents (P) ± standard deviation of percent ($_{(}Sd_P$).

RESULTS AND DISCUSSION

In the SBP daily profile structure the dipper and nondipper types were dominated, similar in frequency and more than 6 times higher than the overdipper and night-peaker incidence.

AH 1 degree was more common among overdippers, and equally less frequently among the other types of daily profile of SBP. AH 2 degree prevailed among nondippers. AH 3 degree prevailed among night-peakers, it was about 4 times higher than among dippers and nondippers. Among overdippers AH 3 degree was absent.

AH stage I was met with equal frequency among dippers and overdippers, accounting about 1/3 of all observations, rarely – among nondippers and wasn't met among night-peakers. AH stage II prevailed among all types of SBP daily profile, amounting in most cases more than half of all observations. AH stage III was met among dippers, nondippers and night-peakers, accounting no more than 1/3–1/5 of all observations.

Patients with HF, which accounted more than half of all observations, prevailed among dippers, nondippers and night-peakers. Among overdippers patients without HF were dominated.

More than half of all patients had HF stage I with the highest frequency of occurrence among night-peakers and the lowest – among overdippers. IIA stage of HF was more common among night-peakers, it was roughly more than twice among dippers and nondippers. Stage IIB was rare and observed only among nondippers.

The incidence of HF FC I prevailed among night-peakers, exceeding such index approximately 2-fold among dippers and overdippers and 3-fold among nondippers. The frequency of HF FC II was higher among nondippers, where it accounted for more than half of all cases. In groups of dippers and night-peakers it was met rarely and with with approximately the same frequency. HF FC III also was observed rarely and only in nondippers.

In the DBP daily profile structure dipper, overdipper and nondipper types were met with approximately the same frequency, whereas night-peaker type was extremely rare.

AH 1 degree absolutely prevailed among night-peakers and accounted for more than half of all cases among overdippers. The incidence of AH 2 degree was more common among dippers, in nondippers it amounted to half of all observations, in overdippers – a little more than 1/3, and in the night-peakers group AH 2 degree wasn't observed. AH 3 degree encountered rarely in all types of DBP daily profile.

AH stage 1 was observed only among dippers and overdippers with low frequency. AH stage 2 prevailed among all four groups, making up in dippers, nondippers and overdippers half or more of all cases, and night-peakers group – 100 %. AH stage 3 was not common among nondippers and even rarer among dippers and overdippers.

Patients with chronic heart failure predominated in all types of DBP daily profile, accounting for more than half of the patients in each group, peaking among nondippers and night-peakers.

Table. 1.

The incidence of AH clinical characteristics depending on the daily BP profile and the selected index of ABPM

ABPM index	BP daily profile	The relative number of patients, P (%) ± standard deviation of percent, Sd_p (%)													
			AH degree			AH stage			No HF	HF FC			HF stage		
			1	2	3	I	II	III		I	II	III	I	II A	II Б
SBP	dipper	42 ± 49,27*	45 ± 49,8*	45 ± 49,8*	9 ± 28,7	32 ± 46,6*	50 ± 50,0*	18 ± 38,6*	27 ± 44,5*	36 ± 48,1*	36 ± 48,1*	0	55 ± 49,8*	18 ± 36,8*	0
	nondipper	47 ± 49,92*	32 ± 46,6*	60 ± 49,0*	8 ± 27,1	12 ± 32,5**	64 ± 48,0*	24 ± 42,7*	20 ± 40,0*	20 ± 40,0*	52 ± 50,0*	8 ± 27,1	60 ± 49,0*	16 ± 36,7*	4 ± 19,6
	night-peaker	6 ± 23,11**	33 ± 47,1	33 ± 47,1	33 ± 47,1	0	67 ± 47,1	33 ± 47,1	0	67 ± 47,1	33 ± 47,1	0	67 ± 47,1	33 ± 47,1	0
	overdipper	6 ± 23,11**	67 ± 47,1	33 ± 47,1	0	33 ± 47,1	67 ± 47,1	0	67 ± 47,1	33 ± 47,1	0	0	33 ± 47,1	0	0
DBP	dipper	32 ± 46,68*	67 ± 47,1	33 ± 47,1	0	0	33 ± 47,1	0	35 ± 47,8*	29 ± 45,6*	24 ± 42,4*	12 ± 32,2	47 ± 49,9*	12 ± 32,2	6 ± 23,5
	nondipper	30 ± 45,91*	31 ± 46,4*	50 ± 50,0*	19 ± 39,0**	0	63 ± 48,4*	38 ± 48,4*	6 ± 24,2	19 ± 39,0**	75 ± 43,3*	0	63 ± 48,4*	31 ± 46,4*	0
	night-peaker	4 ± 19,06	100 ± 0	0	0	0	100 ± 0	0	0	50 ± 50,0	50 ± 50,0	0	100 ± 0	0	0
	overdipper	34 ± 47,36*	56 ± 49,7*	39 ± 48,7*	17 ± 37,3**	39 ± 48,7*	50 ± 50,0*	11 ± 31,4	33 ± 47,1*	39 ± 48,7*	28 ± 44,8	0	56 ± 49,7*	11 ± 31,4	0
PP	dipper	8 ± 26,42*	75 ± 43,3*	25 ± 43,3	0	25 ± 43,3	50 ± 50,0	25 ± 43,3	25 ± 43,3	25 ± 43,3	50 ± 50,0	0	50 ± 50,0	25 ± 43,3	0
	nondipper	34 ± 47,36*	50 ± 50,0*	33 ± 47,1*	17 ± 37,3**	22 ± 41,6*	61 ± 48,7*	17 ± 37,3**	28 ± 44,8*	39 ± 48,7*	28 ± 44,8*	6 ± 22,9	56 ± 49,7*	17 ± 37,3**	0
	night-peaker	55 ± 49,78*	28 ± 44,7*	66 ± 47,5*	7 ± 25,3	21 ± 40,5*	59 ± 49,3*	21 ± 40,5*	21 ± 40,5*	28 ± 44,7*	48 ± 50,0*	3 ± 18,2	62 ± 48,5*	14 ± 34,5*	3 ± 18,5
	overdipper	4 ± 19,06	50 ± 50,0	50 ± 50,0	0	0	50 ± 50,0	50 ± 50,0	50 ± 50,0	0	50 ± 50,0	0	50 ± 50,0	0	0

* $p < 0.05$
** $p < 0.1$

In all groups patients with HF clinical stage I dominated, while a clinical stage IIA was much rarer, and IIB – only in the group of dippers and with a very low frequency.

HF I FC was more common among night-peakers, accounting for half of all cases, prevailed among dippers and overdippers, though rarely met here than in the group of night-peakers, and was rare among nondippers. FC II prevailed in the group of nondippers, met in half of the cases in the group night-peakers and was about ¼ of the groups of overdippers and dippers. FC III observed rarely and only in the dippers group.

In the structure of PP daily profile the night-peaker and nondipper incidence absolutely dominated and the incidence of dipper and overdipper types were rare.

AH 1 degree was more common among dippers, in nondippers and overdippers patients with AH 1 degree accounted for half of all cases, in the group of night-peakers – ¼. AH 2 degree was more common among night-peakers and overdippers, accounting for half and more of all cases, and about 2 times rarely observed among dippers and nondippers. AH 3 degree met rarely and only in groups of nondippers and night-peakers.

AH stage 1 met with low frequency in groups of dippers, night-peakers and nondippers and was absent in overdippers group. AH stage 2 prevailed in all groups of PP daily profile and was half and more of all cases of observation. AH stage 3 was more common in the overdippers and 2–3 times rarely in the other groups.

Patients with chronic heart failure predominated in all groups of PP daily profile, accounting for more than half of all cases in dippers, nondippers and night-peakers and a half – in overdippers group.

In all groups HF clinical stage I dominated, accounting for half and more of all cases. IIA stage occured much less frequently and was at all absent in the overdippers. CHF IIB clinical stage was observed very rarely and only in night-peakers group.

HF I FC prevailed in the group of nondippers, was little rare in dippers and night-peakers and was absent in overdippers group. FC II of CHF prevailed among dippers, night-peakers and overdippers and was almost 2 times less common in nondippers. FC III met rarely, only in groups of nondippers and night-peakers.

The results obtained with regard to SBP circadian BP profile generally confirm the data that the pathological types of circadian BP profile result in the development of complications [10], but the AH clinical signs frequency characteristics, depending on the type of daily profile of SBP, DBP and PP have not previously been studied.

Thus, in this study we received the new data indicating that the frequency characteristics of AH clinical signs vary not only depending on the type of circadian blood pressure profile, but on the selected ABPM index also. Determination of daily profile of DBP and PP carries additional information about the course of the disease and should be performed in all patients with AH.

CONCLUSIONS

AH 1 degree was more common among SBP-overdippers, DBP-night-peakers and PP-dippers, and AH 2 degree – among SBP-nondippers, DBP-dippers and PP-night-peakers, which as a whole accounted for more than half of all cases. AH 3 degree met more common only among the SBP-night-peakers, where it accounted for 1/3 of the observations.

The highest incidence of AH stage I was noted in the group of DBP-overdippers. Stage II prevailed in all groups of patients, accounting for half and more of all cases, with minor differences between the groups. Stage III was more common among PP-overdippers.

Patients with chronic HF prevailed and accounted for more than half of all cases in the vast majority of patients groups, with the highest incidence among SBP- and DBP-night-peakers and DBP-nondippers. I stage of HF significantly prevailed in all groups, accounting for half and more of all cases. Stage IIA was more common among SBP-night-peakers and DBP-nondippers, III stage – among SAD-nondippers, DBP-dippers and PP-night-peakers and didn't exceed 1/10 of all cases. Chronic HF FC I met with the greatest frequency in groups of SBP- and DBP-night-peakers, II FC – in the group of DBP-nondippers, III FC - among DBP-dippers.

Different frequency ratio of AH clinical signs dependently of SBP, DBP and PP daily profiles requires that in AH diagnosis, prognosis and monitoring of treatment all their multitude should be takeт into consideration, but not only SBP diurnal profiles alone.

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A REACTION OF HEART RATE VARIABILITY SPECTRAL PARAMETERS IN THE PHARMACOLOGICAL TEST WITH MEBICAR IN HEALTHY VOLUNTEERS

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On 13 conditionally healthy volunteers aged from 18 to 46 years (mean age – 22±7,6 years) the variability of the total power (TP, ms2) of the spectrum, very low frequency (VLF, ms2), low frequency (LF, ms2) and high frequency (HF, ms2) domains of heart rate variability (HRV) in 5 minute intervals of ECG in I standard lead before and 30 minutes after oral admission of 500 mg of mebicar were evaluated. The data were processed by methods of nonparametric statistics. No significant changes in TP, VLF, LF, HF HRV after 30 minutes (maximum time declared by pharmacodynamics action) after administration of 500 mg of mebicar were noted by us. Accordingly, the effectiveness of mebicar as an adaptogen without evidence-based research cannot be postulated.

KEY WORDS: mebicar, adaptogen, healthy volunteers, pharmacological test

РЕАКЦІЯ СПЕКТРАЛЬНИХ ПАРАМЕТРІВ ВАРІАБЕЛЬНОСТІ СЕРЦЕВОГО РИТМУ У ФАРМАКОЛОГІЧНІЙ ПРОБІ З МЕБІКАРОМ У ЗДОРОВИХ ДОБРОВОЛЬЦІВ

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На 13-ти умовно здорових добровольцях у віці від 18 до 46 років (середній вік – 22 ± 7,6 років) оцінена мінливість загальної потужності спектра (ТР, мс^2), потужностей дуже низькочастотного (VLF, мс^2), низькочастотного (LF, мс^2) і високочастотного (HF, мс^2) домену спектра варіабельності серцевого ритму (ВСР) в 5-хвилинних інтервалах ЕКГ в I стандартному відведенні до і через 30 хвилин після перорального прийому 500 мг мебікару. Дані оброблялися методами непараметричної статистики. Достовірних змін ТР, VLF, LF, HF ВСР через 30 хвилин (декларований час максимуму фармакодинамічної дії) після прийому мебікару в дозі 500 мг нами відзначено не було. Відповідно до цього ефективність мебікару як адаптогена без проведення доказових досліджень не може бути постульована.

КЛЮЧОВІ СЛОВА: мебікар, адаптоген, здорові добровольці, фармакологічна проба

РЕАКЦИЯ СПЕКТРАЛЬНЫХ ПАРАМЕТРОВ ВАРИАБЕЛЬНОСТИ СЕРДЕЧНОГО РИТМА В ФАРМАКОЛОГИЧЕСКОЙ ПРОБЕ С МЕБИКАРОМ У ЗДОРОВЫХ ДОБРОВОЛЬЦЕВ

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На 13-ти условно здоровых добровольцах в возрасте от 18 до 46 лет (средний возраст – 22 ± 7,6 лет) оценена изменчивость общей мощности спектра (ТР, мс^2), мощностей очень низкочастотного (VLF, мс^2), низкочастотного (LF, мс^2) и высокочастотного домена спектра (HF, мс^2) вариабельности сердечного ритма (ВСР) в 5-минутных интервалах ЭКГ в I стандартном отведении до и через 30 минут после перорального приёма 500 мг мебикара. Данные обрабатывались методами непараметрической статистики. Достоверных изменений в ТР, VLF, LF, HF ВСР спустя 30 минут (декларируемое время максимума фармакодинамического действия) после приема мебикара в дозе 500 мг нами отмечено не было. В соответствии с этим эффективность мебикара как адаптогена без проведения доказательных исследований не может постулироваться.

КЛЮЧЕВЫЕ СЛОВА: мебикар, адаптоген, здоровые добровольцы, фармакологическая проба

INTRODUCTION

The global pharmaceutical industry in recent years devotes more and more attention

to various adaptogens that contribute easier carrying of daily life distress [1].

Mebicar positioned as a drug that can affect the serotonergic system of the body and exert anxiolytic, mild sedative and expressed nootropic effect [2–3]. These effects should ensure the rapid restoration of the balance of the regulatory systems of the body, however there is the views about low efficiency of the drug.

Among noninvasive methods to assess autonomic nervous system regulation of heart activity measurement of heart rate variability (HRV) is the most informative and widely used in clinical practice [4].

Given the direct dependence of the adaptive capacities of the organism from the state of regulatory systems [5–6], it is of interest to evaluate their variability in the pharmacological test with mebicar in healthy volunteers.

The study was performed as a part of KhNU research «Development and research of system of automatic control of heart rate variability», № registration 0109U000622.

OBJECTIVE

The purpose of the study was to evaluate the reaction of spectral parameters of HRV in the pharmacological test with mebicar in healthy volunteers.

MATERIALS AND METHODS

The study included 13 conditionally healthy volunteers from 18 to 46 years (mean age – 22 ± 7,6 years). Exclusion criteria were: bad habits, taking medications during last 3 months, resting heart rate less than 60 beats/min, blood pressure less than 100/60 mm Hg.

In accordance with the purpose of the study, in all volunteers were conducted registration of HRV before and 30 minutes after oral admission of 500 mg of mebicar when it [7] reaches peak concentration in the body and when it maximum pharmacodynamics action is declared.

HRV indices were estimated in 5-minute intervals of ECG in the I standard lead in computer-diagnostic complex CardioLab 2009: total power (TP, ms^2), powers of very low frequency (VLF, ms^2), low frequency (LF, ms^2) and the high frequency (HF, ms^2) domains of spectrum [8].

Statistical analysis was performed by using Microsoft Excel. In the table were recorded average values (M) and standard deviations (sd) of TP, VLF, LF, HF on each volunteer before and after ingestion of the drug. The significance of differences of each of the indexes was determined by using the Wilcoxon T-test.

RESULTS AND DISCUSSION

The study included 13 conditionally healthy volunteers from 18 to 46 years (mean age – 22 ± 7,6 years). Exclusion criteria were: bad habits, taking medications during last 3 months, resting heart rate less than 60 beats/min, blood pressure less than 100/60 mm Hg.

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Table

HRV values before (1) and 30 minutes after (2) reception of mebicar in healthy volunteers (M ± sd)

Indexes	Phases of research	
	1	2
TP, ms^2	2715,08 ± 1800,15	4893,08 ± 5046,70
VLF, ms^2	805,54 ± 617,30	1832,23 ± 2269,48
LF, ms^2	1217,77 ± 911,33	2139,69 ± 2513,29
HF, ms^2	604,23 ± 471,64	872,23 ± 850,55

Notes: * – $p < 0,01$ against baseline values.

Mebicar is widely promoted as an effective means of increasing the body's adaptive mechanisms that are implemented by the serotonergic system for the prevention of chronic distress is constantly growing modern living conditions [9–10]. These effects should be mediated in changes of HRV, which, however, were unable to confirm in the present study: before and 30 minutes after administration of 500 mg of mebicar in healthy volunteers values of TP, VLF, LF and HF of HRV were not significantly different, which allows doubt, at least in the quick effect of the drug on the body's regulatory system and its effectiveness as an adaptogen without evidence-based research cannot be postulated.

CONCLUSIONS

1. Mebicar in the dose of 500 mg after 30 minutes (declared time of pharmaco-dynamics action maximum) after a single admission had no significant effect on the TP, VLF, LF, HF of HRV in healthy volunteers.
2. Ability to use mebicar as an adaptogen without evidence-based research cannot be postulated.

PROSPECTS FOR FUTURE STUDIES

It is interesting to evaluate the volatility of HRV parameters in healthy volunteers with a long reception of mebicar.

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HEART ELECTRICAL AXIS α ANGLE VALUES DISTRIBUTION IN PATIENTS, UNDERGOING PERMANENT PACEMAKER IMPLANTATION

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52 patients (24 male and 28 female) aged 71 ± 8 years, underwent permanent pacemaker implantation were included in the study. Analysis of heart electrical axis (HEA) α angle values distribution was carried out in three dimensions in patience before and after pacemaker (PM) implantation. The data processed in Microsoft Excel with calculation of the average and it's standard deviation. Significance of differences in data before and after PM implantation was assessed using Friedman ANOVA test and Kendall concordance coefficient. It was found, that α angle values distribution in patients with implanted PM is transformed from a unimodal to bimodal on the permanent cardiac pacing background. It's assumed, that α angle changes resulting due to right ventricular electrode positioning options during PM implantation. Clarification of the nature of this change requires a special study.

KEY WORDS: permanent cardiac pacing, heart electrical axis

РОЗПОДІЛЕННЯ ЗНАЧЕНЬ КУТА α ЕЛЕКТРИЧНОЇ ОСІ СЕРЦЯ У ПАЦІЄНТІВ З ПОСТІЙНОЮ ЕЛЕКТРОКАРДІОСТИМУЛЯЦІЄЮ

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Обстежено 52 пацієнта (24 чоловіка і 28 жінок) у віці 71 ± 8 років, які піддалися імплантації постійного електрокардіостимулятора. Проводився аналіз змін розподілу значень кута α електричної осі серця (ЕОС) в трьох площинах до і на тлі постійної електрокардіостимуляції (ЕКС). Вивчалися розподіл значень кута α в популяції пацієнтів до і після імплантації ЕКС. Дані оброблялися в Microsoft Excel з розрахунком середнього і його стандартного відхилення. Достовірність відмінностей в даних до і після імплантації ЕКС оцінювалася з використанням тесту Фрідмана ANOVA і коефіцієнта конкордації Кендала. Виявлено, що розподіл значень кута α у пацієнтів з імплантованими ЕКС трансформується з одномодального в бімодальне на тлі постійної ЕКС. Допускається, що отримані зміни кута α обумовлені варіантами позиціонування правошлуночкового електрода при імплантації електрокардіостимулятора. Уточнення природи змін вимагає спеціального дослідження.

КЛЮЧОВІ СЛОВА: постійна електрокардіостимуляція, електрична вісь серця

РАСПРЕДЕЛЕНИЯ ЗНАЧЕНИЙ УГЛА α ЭЛЕКТРИЧЕСКОЙ ОСИ СЕРДЦА У ПАЦИЕНТОВ, ПОДВЕРГШИХСЯ ИМПЛАНТАЦИИ ПОСТОЯННОГО ЭЛЕКТРОКАРДИОСТИМУЛЯТОРА

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Обследованы 52 пациента (24 мужчины и 28 женщин) в возрасте 71 ± 8 лет, подвергшихся имплантации постоянного электрокардиостимулятора. Проводился анализ изменений распределения значений угла α электрической оси сердца (ЭОС) в трех плоскостях до и на фоне постоянной

электрокардиостимуляции (ЭКС). Изучались распределения значений угла α в популяции пациентов до и после имплантации ЭКС. Данные обрабатывались в Microsoft Excel с расчетом среднего и его стандартного отклонения. Достоверность различий в данных до и после имплантации ЭКС оценивалась с использованием теста Фридмана ANOVA и коэффициента конкордации Кендала. Выявлено, что распределение значений угла α у пациентов с имплантированными ЭКС трансформируется из одномодального до в бимодальное на фоне постоянной ЭКС. Допускается, что полученные изменения угла α обусловлены вариантами позиционирования правожелудочкового электрода при имплантации электрокардиостимулятора. Уточнение природы изменений требует специального исследования.

КЛЮЧЕВЫЕ СЛОВА: постоянная электрокардиостимуляция, электрическая ось сердца

INTRODUCTION

The most widely used and effective treatment of hemodynamically significant bradyarrhythmias is permanent cardiac pacing (CP) [1–3]. It, however, does not solve the problem of associated cardiovascular pathologies and requires therapeutic monitoring [1–2, 4].

One of the most important electrophysiological parameters of heart condition in a variety of cardiovascular diseases is a heart electric axis (HEA) [5]. The most informative HEA reflection is projection of α angle on the frontal, sagittal and horizontal dimensions [6]. Unconditional effect on EOS, among other indicators, provides a permanent pacemaker [7], but its a little literature on this topic.

OBJECTIVE

Aim of this work is analysis of heart electrical axis α angle values distribution in patience, undergoing permanent pacemaker implantation.

MATERIALS AND METHODS

52 patients aged 71 ± 8 (M ± sd) (28 – female, 24 – male) were examined in the department of ultrasound and instrumental diagnostics with miniinvasive interventions of GI «Zaycev V. T. Institute of General and Urgent Surgery of NAMS of Ukraine». All patients were underwent permanent pacing therapy from 2006 to 2015 in modes: DDD (21 patients) and DDDR (15 patients), VVI (12 patients), VVIR (5 patients).

Patience younger than 40 years, with concomitant stable angina IV functional class (FC), chronic heart failure (CHF) IV FC and/or stage III with right ventricular (RV) pacing and/or left ventricular (LV) pacing less than 50 % of all rhythm was excluded from investigation.

Value of α angle in a frontal, sagittal and horizontal plane projection was evaluated before pacemaker implantation and in acute postoperative period (3–5 days).

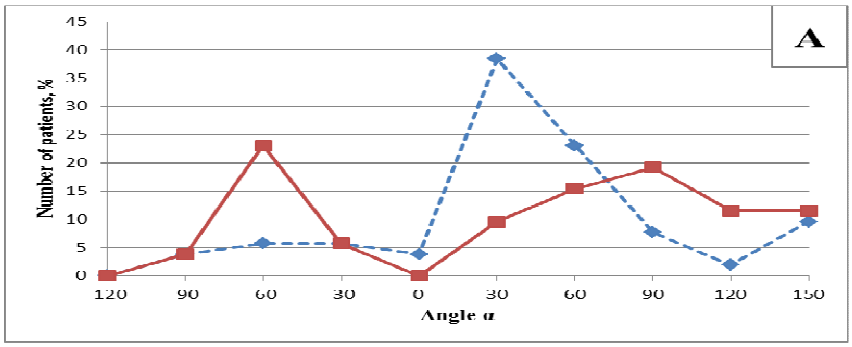
Electrocardiography registration were carry out to all patience on a computer ECG electrocardiograph «Cardiolab +» (HAI-Medica). Computer program «Cardiolab Imp» (HAI-Medica) were used for measuring an angle values. The α angle value is evaluated by the median complex for a 5 seconds period from 12 standard ECG leads.

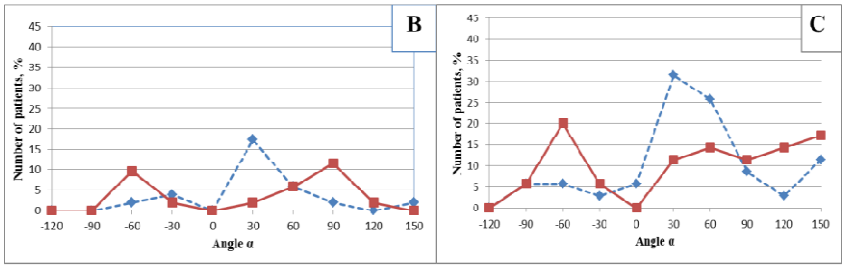
5 classes of electrical axis position (EAP) were allocated according to α angle values: normal – $\alpha = 30–70^{o}$, horizontal – $\alpha = 0–30^{\circ}$, vertical – $\alpha = 70–90^{o}$, right deviation – $\alpha > 120^{\circ}$, left deviation – $\alpha < 0^{\circ}$. α angle distribution values were studied in patients' population in all three dimensions before and after pacemaker implantation.

The data were processed after formation the Microsoft Excel using standard statistic procedure (for parametric data: mean – M, standard deviation – sd, for nonparametric ones: absolute (n, number) and relative (percentage of (p, %). The probability of differences of α angle values before and after PM implantation was determined using Friedman ANOVA test and Kendall concordance coefficient. The expected result is determined by level of reliability $p < 0.05$.

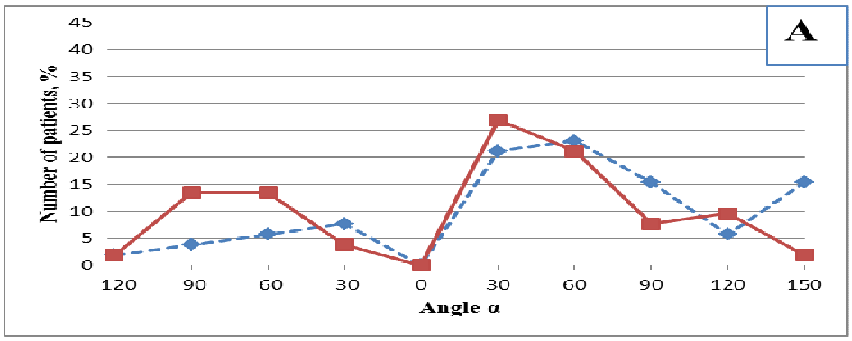
RESULTS AND DISCUSSION

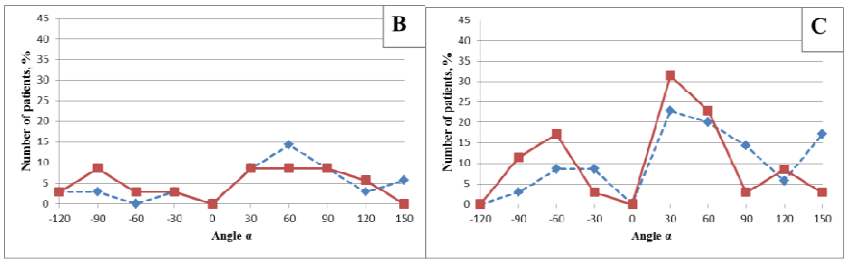
α angle values distribution in a frontal, sagittal, horizontal dimensions before and after PM implantation in the general population, in patients with VVI/VVIR and patients with DDD/DDDR pacemakers are shown in fig. 1.


A
Number of patients, %
Angle α

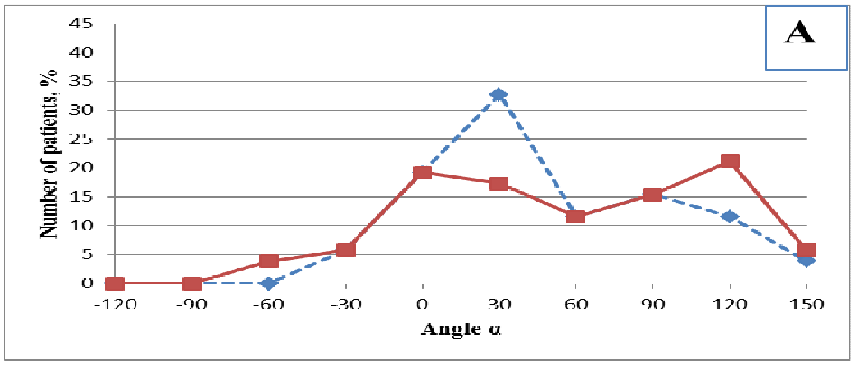

B
C
Number of patients, %
Angle α

II


A
Number of patients, %
Angle α


B
C
Number of patients, %
Angle α

III


A
Number of patients, %
Angle α

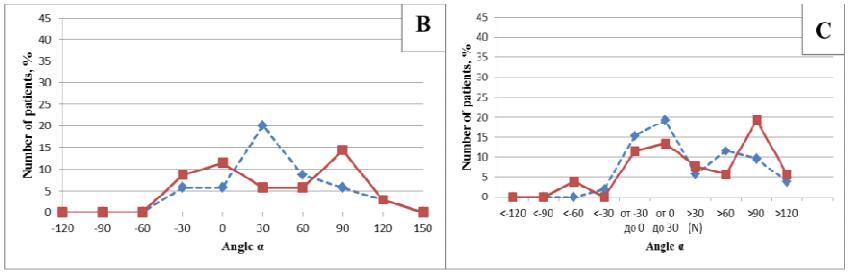


Fig. 1. α angle values distribution in a frontal (I), sagittal (II), horizontal (III) dimensions before and after PM implantation in the general population (A), in patients with VVI/VVIR (B) and patients with DDD/DDDR pacemakers (C)

α angle values distribution in all patience in a frontal dimension was unimodal in class of horizontal EAP before PM implantation (0 to 30°). α angle values distribution became bimodal during permanent cardiac pacing, with peaks in classes of EAP displacement to the left (α < 0°) and to the right (α > 90°).

α angle values distribution in sagittal and horizontal dimensions were close to bimodal, both before and after implantation of the pacemaker with maxima in classes of normal EAP (30 to 70°) and horizontal EAP (0 to 30°) positions, before it's left (α < 0°) and right (α > 90°) deviation after PM implantation. Installed changes in α angle values distribution of EAP with pacemaker implantation in all three dimensions were statistically significant at $p < 0.05$.

EAP is an important diagnostic sign of heart condition in a variety of cardiovascular diseases, followed by as a ventricular myocardial hypertrophy, intraventricular conduction disturbances, focal lesions of the myocardium [8], as a permanent PM implantation [7], and so its regular assessment has an important clinical implications. Our data on α angle values distribution in frontal, sagittal and horizontal planes in the studied group of patients before PM implantation characteristic of patients with coronary heart disease, hypertension, atrial fibrillation, congestive heart failure, diabetes, according to literature data [5, 8].

Referring variants we found of two α angle deviation, and so on EAP, in patients during permanent cardiac pacing, left and right, respectively, it can be noted that such data is not available in the literature. Most likely, the received changes of positioning options were seen due to right ventricular pacing electrode position, which, however, requires a special study [9].

The same patterns of change in α angle values distribution after PM implantation in all dimensions and most informative it's projection onto the frontal dimension give grounds to limit the results of this plane for practical purposes.

The fact of the transformation of unimodal α angle distribution in bimodal with a change in the maximum from the class of normal EAP highs in displacement for classes of left and right EAP deviation in the studied group of patients sets the task to study it's possible values in the changing health status of patients with implanted PM.

CONCLUSIONS

1. α angle values distribution in patients with implanted PM transformed from a unimodal to bimodal on the background of permanent cardiac pacing.
2. Changing of α angle values distribution in patients with implanted PM occurs in all three dimensions, turning out the most informative in the frontal dimension.
3. Determination of α angle values distribution changes in patients with implanted permanent PM may have diagnostic value and therefore requires dynamic control.
4. It's a quite limited to control α angle values changes in the frontal plane in clinical practice.

PROSPECTS FOR FUTURE STUDIES

It seems appropriate to investigate the links in the nature of changes of heart's electrical axis position with the health changes in patients with implanted permanent pacemaker.

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Clinical case

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PASSIONS AROUND PHEOCHROMOCYTOMA

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A clinical case of arterial hypertension (AH) in patient with family history of pheochromocytoma is described. Patient has no classical clinical signs and imaging phenotype of pheochromocytoma, but there are a number of warnings – family history of pheochromocytoma, prevalence of humoral-metabolic regulation and reduced reaction to the respiratory test, CT-signs of nodular hyperplasia of left adrenal gland – which may indicate its possible manifestations in the future, and therefore the monitoring is required.

KEY WORDS: arterial hypertension, pheochromocytoma, clinical case

ПРИСТРАСТІ НАВКОЛО ФЕОХРОМОЦИТОМИ

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Описаний випадок артеріальної гіпертензії (АГ) у пацієнта з сімейним анамнезом феохромоцитоми. У пацієнта відсутні класичні клінічні симптоми цього захворювання, а також характерні для феохромоцитоми зміни на комп'ютерній томограмі (КТ). Однак виявлено ряд ознак, які свідчать про її можливий розвиток в майбутньому – обтяжена по феохромоцитомі спадковість, переважання гуморально-метаболічної регуляції і знижена реакція на дихальну пробу, КТ-ознаки нодулярної гіперплазії лівого надниркика, у зв'язку з чим пацієнт потребує спостереження.

КЛЮЧОВІ СЛОВА: артеріальна гіпертензія, феохромоцитома, клінічний випадок

СТРАСТИ ВОКРУГ ФЕОХРОМОЦИТОМЫ

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Описан случай артериальной гипертензии у пациента с семейным анамнезом феохромоцитомы. У пациента отсутствуют классические клинические симптомы этого заболевания, а также характерные для феохромоцитомы изменения на компьютерной томограмме (КТ). Однако выявлен ряд признаков, свидетельствующих о её возможном развитии в будущем – отягощенная по феохромоцитоме наследственность, преобладание гуморально-метаболической регуляции и сниженная реакция на дыхательную пробу, КТ-признаки нодулярной гиперплазии левого надпочечника, в связи с чем пациент нуждается в наблюдении.

КЛЮЧЕВЫЕ СЛОВА: артериальная гипертензия, феохромоцитома, клинический случай

INTRODUCTION

Patient D. with arterial hypertension (AH), whose mother suffer from pheochromocytoma [1, 2], presented to the Department of Internal Medicine with worrying that his high blood pressure (BP) can be due to the same problem.

He is 37 years old, employee of the security company, in the past - a professional wrestler.

COMPLAINTS

Increased blood pressure, tachycardia episodes and headache of pulsating nature while exercising in the gym.

ANAMNESIS MORBI

Patient started monitoring himself with a home blood pressure monitor at the age of 25 after the diagnosis of his mother with pheochromocytoma. BP readings did not exceed 140/90 mm Hg. Since the age of 30

there were episodes of tachycardia and headaches during training in the gym. BP levels periodically increased up to 160/100 mm Hg, without any accompanying symptoms. In 2014 was examined in National Institute of Therapy named by L. T. Malaya, where the diagnosis was made: Essential Arterial Hypertension, II st., with sympathetic-adrenal paroxysms. «Normatens» 1 tablet at bedtime and carvedilol 12,5 mg 2 times daily under HR control were recommended.

In additional questioning weight loss, episodes of excessive sweating, accompanied by tremors, fever and headache, and symptoms of orthostatic hypotension denied. Episodes of tachycardia and throbbing headache occur only on a background of heavy physical exertion, resolved at rest within 20–30 minutes after exercise discontinuance. BP in these moments has not been measured. Severity of symptoms did not change over the last 7 years. BP measuring is performed occasionally (non-daily) at home, at rest. When elevated blood pressure numbers are registered any other accompanying symptoms are not observed.

Presently episodically takes Normatens (when SBP ≥ 160) and «Koriol» (carvedilol) in case of tachicardia. Last 2 months didn't take any medications.

ANAMNESIS VITAE

Smokes approximately 12 cigarettes per day. Feeds regularly and adequately. Three times a week has training in the gym. Denied drug usage and alcohol intake. Father died of sudden cardiac death at age 54. Mother alive, was diagnosed with pheochromocytoma in 2003, not operated.

STATUS PRESENCE OBJECTIVUS

Condition was satisfactory, consciousness clear, patient was active and not in distress. Type of body constitution was hypersthenic. Height – 168 cm, weight – 78 kg, BMI= 27,6 kg/m2. Skin – normal pink color. Peripheral lymph nodes were not palpable. Thyroid lobes were not palpable; the isthmus was palpated as a homogeneous smooth cross-strand, 1 cm wide. Musculoskeletal system examination was unremarkable. Lungs: resonant percussion note, vesicular breathing over the lungs fields, RR 18 bpm. Heart borders were not extended, heart activity was rhythmic with HR of 72 bpm. Heart tones are clear in all auscultating points. No murmurs. Blood pressure measured in the supine position on the left arm – 145/100 mm Hg, on the right arm – 150/105 mm Hg, PS – 72 bpm. 2 minutes after the transition to the upright position BP on both arms 150/100, HR = 78 bpm. Abdomen was of normal size, painless in palpation. Liver was palpated at the costal margin, painless. There was absence of vascular sounds during abdomen auscultation. Pasternatskiy sign was negative on both sides. No peripheral edema.

PLAN OF SURVEY:

Full blood count, Urinalysis, Basic biochemical panel, ECG, Heart Rate Variability, EchoCG, ABPM, Abdominal ultrasound, CT scanning of the kidney, adrenal glands [3].

RESULTS OF INVESTIGATIONS

The white-cell count was 5.2×10^9/l, with 60 % neutrophils, 33 % lymphocytes, 6 % monocytes and 1 % eosinophils. The hemoglobin level was 156 g per liter, the erythrocytes 5.15×10^{12}/l, and the platelet count 262.7×10^9/l. *Erythrocyte sedimentation rate was 1 mm/h. The urinalysis was normal. The basic biochemical panel and liver-function tests were normal. The total cholesterol was elevated at 6.67 mmol/l (normal range ≤ 5.2 mmol/l), very low-density lipoprotein cholesterol 0.37 mmol/l (normal range up to 0.77 mmol/l), low-density lipoprotein cholesterol was elevated at 4.47 mmol/l (normal range up to 3.1 mmol/l), high-density lipoprotein cholesterol 1.48 mmol/l (normal range 0.9–1.55 mmol/l), triglycerides 0.83 mmol/l (normal range < 1.7 mmol/l), atherogenic ratio was elevated at 3.27 (normal range up to 3.0).*

ECG showed sinus rhythm with HR 70 bpm. Heart axis had horizontal position. A nonspecific ST-T change in left ventricular posterior wall was recorded (Fig. 1).

To assess the state of the autonomic nervous system the breathing test was performed. The level of neuro-humoral regulation at rest was low, with the prevalence of humoral-metabolic regulation. The reaction to the respiratory test was reduced (Krr: 1.20), with a slight strengthening of parasympathetic activity (Fig. 2).

The nature of rhythm regulation at rest (after deep breathing) indicated a stabilization of heart rate with the transition of its regulation from the autonomic nervous system level to a lower

humoral-metabolic level of regulation, which is not able to quickly provide homeostasis (fig. 3).

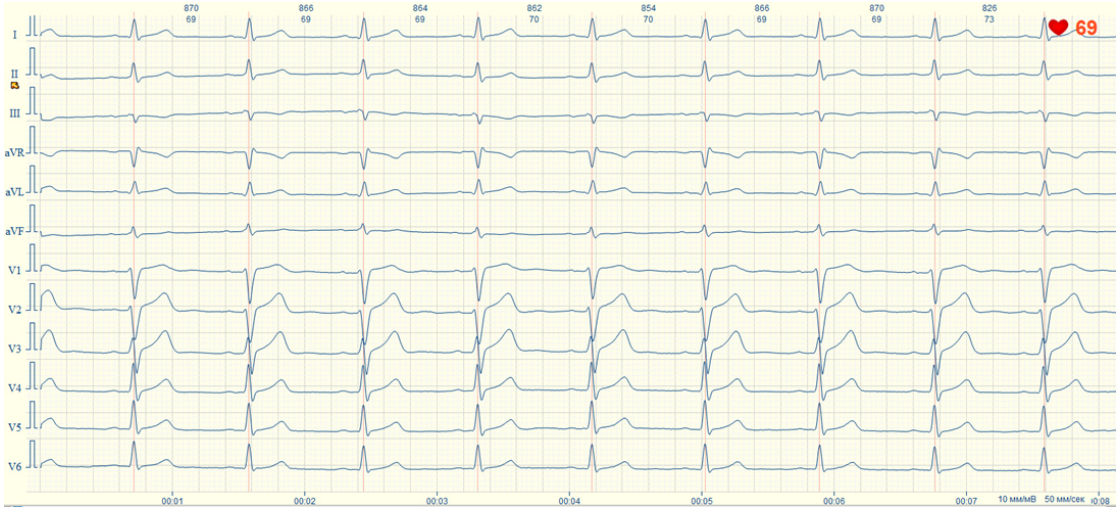

Fig. 1. ECG

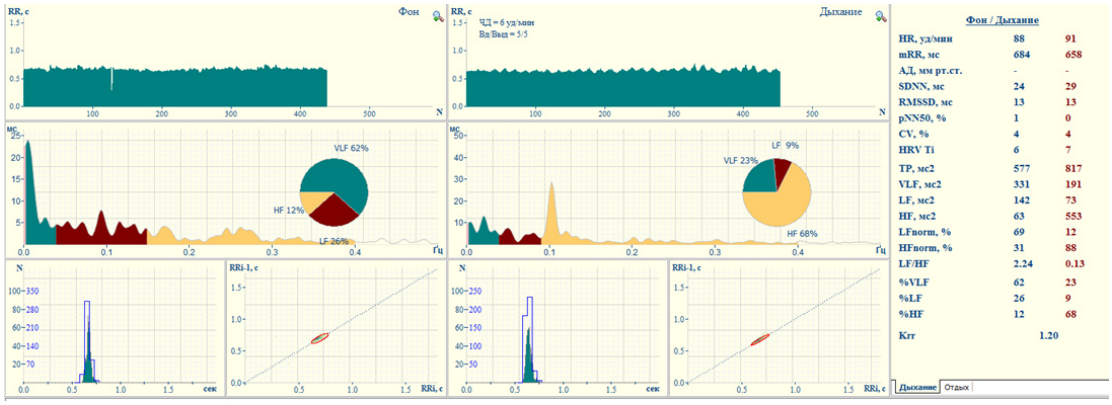

Fig. 2. Breathing test. Base level/breathing

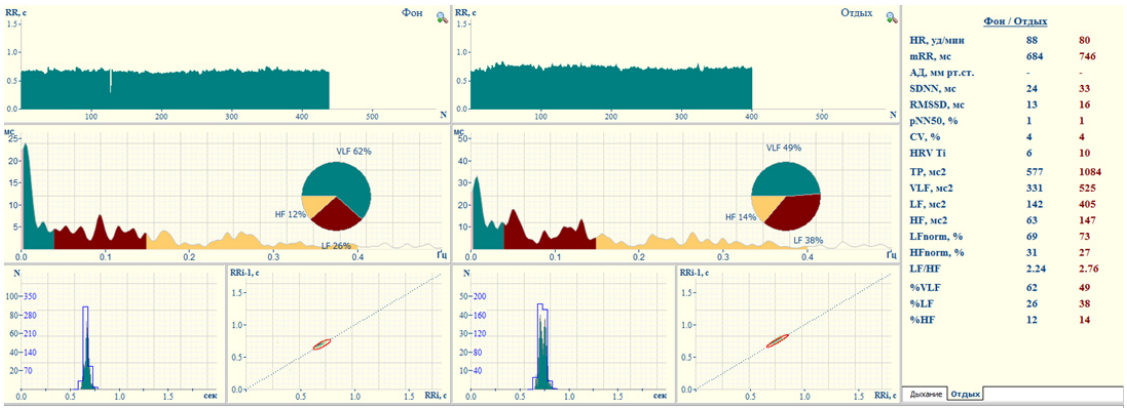

Fig. 3. Breathing test. Breathing / rest

EchoCG showed data indicative of left ventricle (LV) hypertrophy – thickening of the LV posterior wall at 1.56 cm (normal range 0.6-1.2 cm) and intraventricular septum at 1.55 cm (normal range 0.6–1.3 cm) along with increased LV mass at 365.56 g (normal range, men < 183 g) and increased LV mass index at

194.58 g/m^2 (normal range, men < 115 g/m^2 body surface area). Ejection fraction was 60 %.

According to the ABPM data, on the background of the absence of antihypertensive therapy, stable mild systolic 24-h hypertension with a physiological degree of sleep-time relative SBP decline and mild stable awake diastolic hypertension with an excessive fall in DBP at night, with increased variability of SBP and DBP in the 24-h period was recorded. DBP means and variability in SBP and DBP at night in the normal range. The excess MAP sleep-time fall on the background of the normal range during the night and increased - during the day was recorded. Pulse pressure exceeds normal levels during the whole period of monitoring, with a predominance of nocturnal values over the awake ones and the formation of a PAD daily profile of night-peaker type (Tab. 1, 2).

Abdominal ultrasound was unremarkable. Abdominal CT scanning showed adrenal glands, located in a typical place, the right adrenal gland was not enlarged, legs up to 3 mm thick, with clear contours, homogeneous structure. The left adrenal gland was of normal size, with irregularly thickened legs from 3 to 8 mm, with clear contours, homogeneous structure. The surrounding fatty tissue was not changed (Fig. 4, 5). Conclusion: CT-signs of nodular hyperplasia of left adrenal gland.

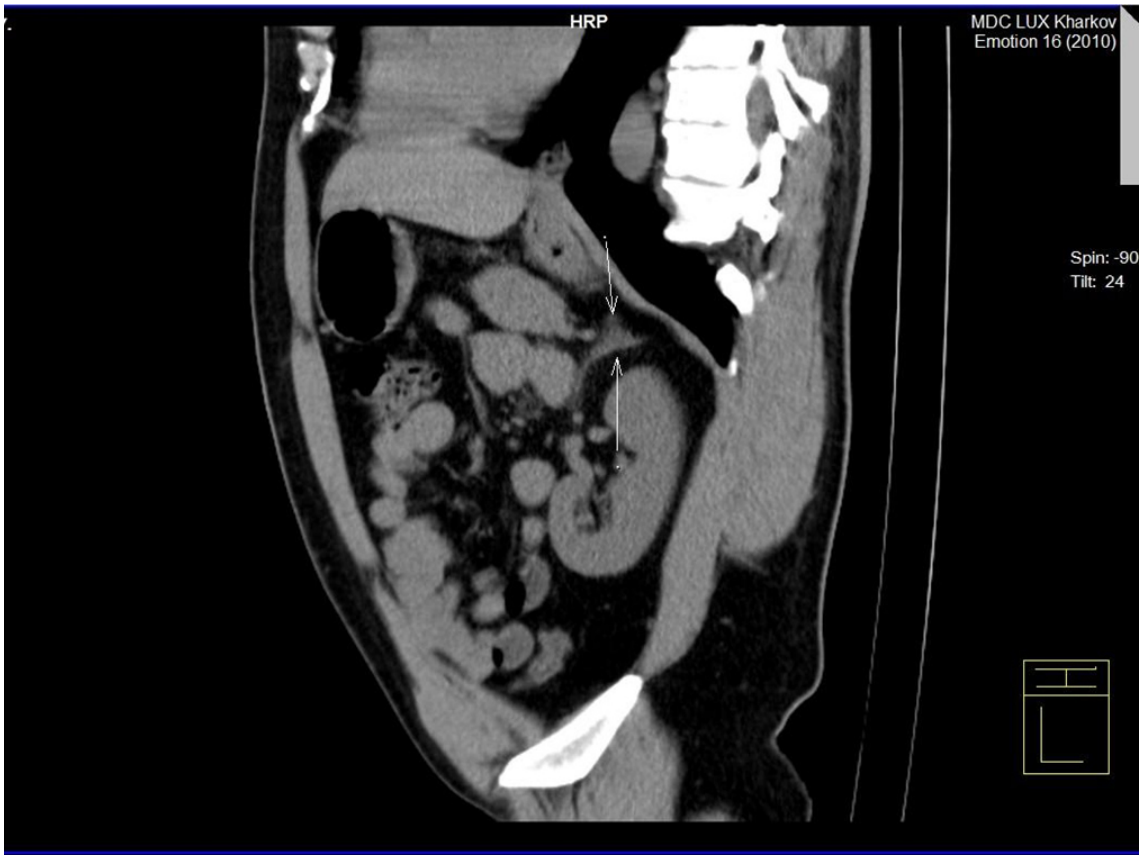

Fig. 4. Left adrenal gland indicated with arrows

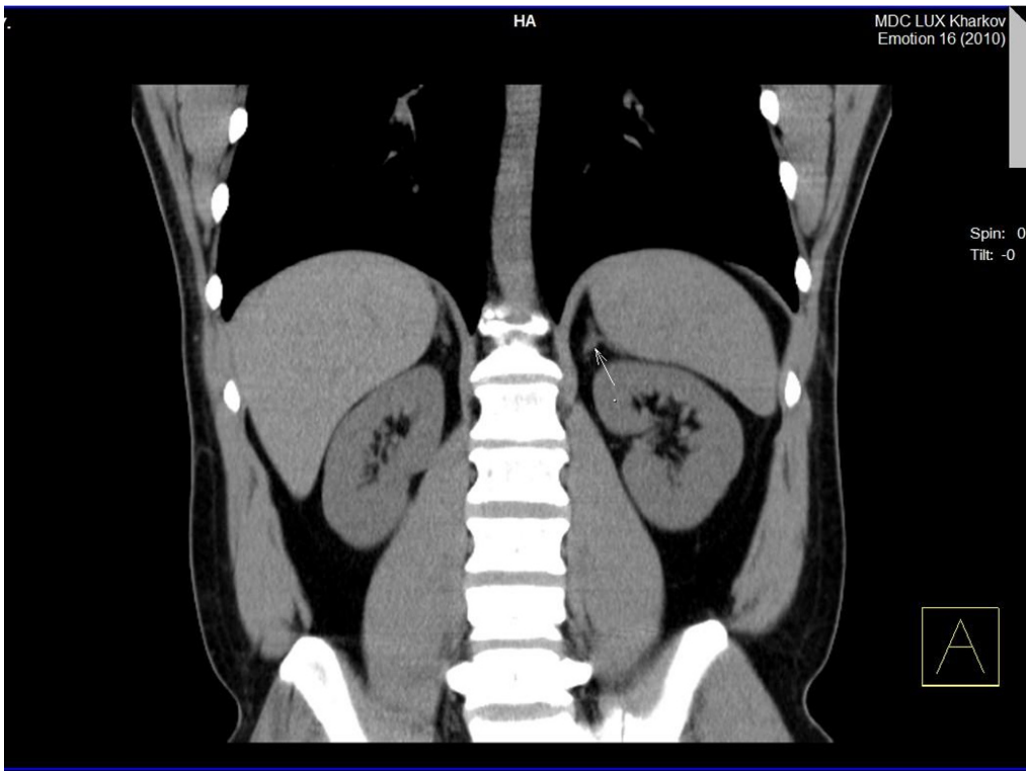

Fig. 5. Left adrenal gland indicated with arrow

Table 1

ABPM means*

Indices	*Patient data*	*Normal Ranges*
24-h PERIOD		
SBP, daily mean, mmHg	142	No more then 130
DBP, daily mean, mmHg	85	No more then 80
MAP, daily mean, mmHg	103	80-95
PAP, daily mean, mmHg	57	Less than 46
SBP time index, %	79.1	Less than 15
DBP time index, %	64.8	Less than 15
SBP variability, mmHg	17.4	No more then 15
DBP variability, mmHg	19.9	No more then 14
MAP variability, mmHg	17.9	*no generally accepted normal values*
PAP variability, mmHg	14.7	*no generally accepted normal values*
AWAKE MEANS		
SBP, awake mean, mmHg	147	No more then 135
DBP, awake mean, mmHg	93	No more then 85
MAP, awake mean, mmHg	110	80-95
PAP, awake mean, mmHg	54	Less than 46
SBP time index, %	84,9	Less than 15
DBP time index, %	81,5	Less than 15
SBP variability, mmHg	16.6	No more then 15
DBP variability, mmHg	17.4	No more then 14
MAP variability, mmHg	14.9	*no generally accepted normal values*
PAP variability, mmHg	16.0	*no generally accepted normal values*
ASLEEP MEANS		
SBP, asleep mean, mmHg	129	No more then 120
DBP, asleep mean, mmHg	65	50-70
MAP, asleep mean, mmHg	84	80-95
PAP, asleep mean, mmHg	64	Less than 46
SBP time index, %	67,7	Less than 15
DBP time index, %	31,9	Less than 15
SBP variability, mmHg	12,0	No more then 15
DBP variability, mmHg	9,6	No more then 14
MAP variability, mmHg	10,0	*no generally accepted normal values*
PAP variability, mmHg	7,4	*no generally accepted normal values*

** SBP – systolic blood pressure, DBP – diastolic blood pressure, MAP – mean arterial pressure, PAP – pulse arterial pressure*

Table 2

Daily BP profiles*

Indices	Profile type	Night-time decline, %
SBP	Dipper	12,5
DBP	Overdipper	29,8
MAP	Overdipper	23,3
PAP	Nightpicker	- 18,5

***** *SBP – systolic blood pressure, DBP – diastolic blood pressure, MAP – mean arterial pressure, PAP – pulse arterial pressure*

The consultation of endocrinologist, measurement of fractionated metanephrines and catecholamines in a 24-hour urine specimen was recommended.

Endocrinologist conclusion: no data for pheochromocytoma. Taking into account data of instrumental methods of investigation, described above, we still recommended to check the level of catecholamines and cortisol in blood and urine.

Motivating with endocrinologist conclusion, the patient refused any further examination.

Taking into account the available data the diagnosis was made:

Arterial hypertension, Grade 2, Stage II (LVH), high risk, with an excessive fall in DBP at night and physiological degree of sleep-time relative SBP decline, with reduced reaction on breathing test, HF 0. Nodular hyperplasia of the left adrenal gland.

The patient was recommended to maintain a healthy lifestyle, smoking cessation, decrease sodium intake, lipid-lowering diet, amlodipine 5 mg in the morning protractedly under the control of blood pressure level.

The patient also was recommended to repeat the ABPM after 3 months, but at the appointed time the patient did not come. In a telephone conversation he said that he feels satisfactory, according to HBPM his BP is within 130–140/85 mm Hg, in further examination and observation he is not interested. It was recommended to continue amlodipine intake, monitoring adrenal hyperplasia using abdominal CT-scanning yearly and measurements adrenal hormones in serum and urine.

CONCLUSIONS

Our patient with AH and family history of pheochromocytoma has no classical clinical signs and imaging phenotype of pheochromocytoma [4], but there are a number of warnings – family history of pheochromocytoma, prevalence of humoral-metabolic regulation and reduced reaction to the respiratory test, CT-signs of nodular hyperplasia of left adrenal gland - which may indicate its possible manifestations in the future, and therefore the monitoring is required.

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MULTICOMPLICATED MYOCARDIAL INFARCTION

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The clinical course of myocardial infarction frequently burdened by a variety of complications, which largely determine its scenario and prognosis. Despite advances in the management of this disease, complications can and do occur. These dangers arise from two principal sources: on the one hand, from the local effects of the lesion and the circulatory depression that follows, and, on the other, from the hazards that may attend during active treatment.

On example of clinical case is demonstrated severe course of myocardial infarction with development of multiple complications at different stages, but, ultimately, with a favorable outcome. Early, aggressive, and judicious treatment of these complications may substantially decrease the morbidity and mortality associated with this disease.

KEY WORDS: myocardial infarction, complications of myocardial infarction

ІНФАРКТ МІОКАРДУ З БЕЗЛІЧЧЮ УСКЛАДНЕНЬ

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Клінічний перебіг інфаркту міокарда часто обтяжується різними ускладненнями, які значною мірою визначають його сценарій і прогноз. Незважаючи на успіхи в лікуванні цього захворювання, ускладнення можуть траплятися і трапляються. Ці загрози виникають з двох основних джерел: з одного боку – це локальні ефекти вогнища ураження і подальша декомпенсація кровообігу, з іншого – це ризики, пов'язані з активним лікуванням.

На прикладі клінічного випадку розглядається важкий перебіг інфаркту міокарда з розвитком безліч ускладнень на різних етапах, проте, у кінцевому підсумку, зі сприятливим кінцем. Раннє, агресивне і розумне лікування цих ускладнень може істотно знизити важкість перебігу і смертність, пов'язані з цим захворюванням.

КЛЮЧОВІ СЛОВА: інфаркт міокарду, ускладнення інфаркту міокарда

ИНФАРКТ МИОКАРДА С МНОЖЕСТВОМ ОСЛОЖНЕНИЙ

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Клиническое течение инфаркта миокарда зачастую отягощается множеством осложнений, которые, в свою очередь, определяют его сценарий и прогноз. Несмотря на достижения в лечении данной патологии, осложнения могут и продолжают встречаться. Эти угрозы возникают из двух основных источников: с одной стороны – это локальные эффекты очага поражения и последующая декомпенсация кровообращения, с другой – это опасности, связанные с активным лечением.

На примере клинического случая рассматривается тяжелое течение инфаркта миокарда с развитием множества осложнений на разных этапах, однако, в конечном итоге, с благоприятным исходом. Раннее, агрессивное и разумное лечение этих осложнений может существенно снизить тяжесть течения и смертность, связанные с этим заболеванием.

КЛЮЧЕВЫЕ СЛОВА: инфаркт миокарда, осложнения инфаркта миокарда

INTRODUCTION

The clinical course of myocardial infarction frequently burdened by a variety of complications, which largely determine its scenario and prognosis [1]. Complications are different and life threatening. Despite advances in the

management of this disease, complications can and do occur.

Acute myocardial infarction frequently takes life in the first hour after a heart attack, before qualified medical aid is provided. If a person survives the sudden loss part of the ventricular muscle due to ischemic necrosis, there follows a period in which special dangers threaten each of the physical systems and the personality itself [2]. These dangers arise from two principal sources: on the one hand, from the local effects of the lesion and the circulatory depression that follows, and, on the other, from the hazards that may attend during active treatment [2]. Development of complications are determined not only by the size of lesion, but also a combination of conditions (first of all, the state of the myocardium on the background of atherosclerosis of the coronary arteries, prior myocardial diseases, presence of electrolyte abnormalities) [1].The onset of each of these complications usually results in explicit symptoms and physical manifestations. Thus, a basic knowledge of the complications that occur in the postinfarction period and the clinical syndromes associated with each, will allow the physician to evaluate and treat the complication appropriately. Prompt diagnosis and therapy are life-saving. Outcome of patients with myocardial infarction is determined by the complications that develop in the early and late stages of the disease.

Main purpose of the doctor to create conditions for uncomplicated healing of lesion, prevent inadequate stress response – distress [3]. The mechanism of complications is always the same: desynchronization of necrotic and reparative processes [3].

On example of clinical case is demonstrated severe course of myocardial infarction with development of multiple complications: on the one hand, from the focal necrosis of the heart muscle and the pump dysfunction that ensue, and, on the other, from the side effects that accompany active treatment. In this incident the severity of complications exceeded the severity of myocardial infarction itself. It needed the set of interventions to take out the patient from such grave condition.

OBJECTIVE

The purpose of this article is to represent the complications that may arise in the course of acute MI and demonstrate that various therapeutic modalities, both medical and surgical, should be able to improve not only symptoms but also survival of the patient.

CLINICAL CASE

65 years old retired male, resident of urban area.

COMPLAINTS

Patient complain of burning central chest pain, more than 60 min duration, without any radiation, nitroglycerine intake doesn't relief pain, abrupt onset, severity 7; and dyspnea at rest, exacerbated by minimal physical exertion

PRESENT ILLNESS

Central chest pain and worsening symptoms of dyspnea had been appeared abruptly, when the patient was at home and carried out household chores. Patient took nitroglycerine three times, but it did not relief pain. After 30 min patient had called to emergency. ECG had been recorded. Signs of STEMI of the posterior wall had been found and patient had been delivered to cardiologic emergency department.

PAST MEDICAL HISTORY

Over 20 years patient suffer from essential hypertension. Patient said that prescribed by cardiologist medications (ACE inhibitors, diuretics and b-blockers) had been taken regularly, but BP level had not been controlled properly (it occurred rising of BP to 160–200/100 mm Hg).

In 1999 patient underwent left internal carotid endarterectomy was carried out because of carotid artery atherosclerosis.

Since 2003 year bother persistent atrial fibrillation tachysystolic form, which on repeated occasions was successfully converted to sinus rhythm by pharmacologic cardioversion (IV amiodarone)?

25.02.2010 patient had STEMI inferior wall complicated by cardiogenic shock, Dressler's syndrome.

06.12.2010 patient had ischemic stroke in the circle of Willis.

DRUG HISTORY

Patient intake following medicines, prescribed by cardiologist: nebivalol 5 mg per day, losartan 50 mg per day, hydrochlorothiazide 25 mg per day, aspirin 75 mg per

day, clopidogrel 75 mg per day, atorvastatin 20 mg pd.

FAMILY HISTORY

Patient's mother and brother suffer from essential hypertension.

ALCOHOL AND SMOKING

Patient intake about 1,5 L of normal beer per day, equivalent 42 units of alcohol per week.

Patient smoke 1,5–2 packs of cigarettes per day during 40 years, which equals 60–80 pack-years.

INSPECTION

Vital sings:
Body temperature – 36,8 °C
PS – 40 bpm
BP – 110/60 mm Hg
Respiratory rate – 17 pm
High – 188 cm
Weight – 105 kg
BMI – 30,2 kg/m2

Elderly male, has correct orientation in space and surroundings, mild depressed. The posture is orthopnea (the patient uses 3 pillows). Skin is pale, mild cyanosis of the lips, fingers and toes, rashes and hemorrhages are absent. Turgor and elasticity of the skin is decreased. Subcutaneous fat tissue is increased, predominantly in abdominal zone (central obesity, waist circumflex 138 cm). Nails are without any abnormalities. Mucous membranes are pale and wet. Tongue is clear and wet. Severe edema of the low extremities (3+). Lymph nodes are not palpable. Joints are normal, active and passive movements are painless. The head and neck examination is normal. Carotid pulsation. JVP 6,5 cm above the sternal angle. The chest is normal shape. Decrease breath sounds and bibasilar coarse crackles of the lungs to auscultation. The point of apex beat is diffuse, 3 cm in diameter, shifted to the left (palpated 1,5–2 cm to the left from midclavicular line in the 5th intercostal space). S1 and S2 are soft. Holosystolic murmur best heard at the tricuspid valve. Abdomen is soft and nontender. Hepatomegaly (+ 4 cm), liver palpation is tender. The kidneys are not palpable. Stool is normal. Urination is normal.

CLINICAL DATA

At the time of admission to the hospital complete blood count detected neutrophilic leukocytosis (WBC 11.8 10*9/L, NE 9.1 10*9/L, 77,8 %); urine analysis – mild proteinuria (0.068 g/L); biochemical blood profile revealed normal ranges of serum glucose (4.1 mmol/L) and bilirubin (9.98 mkmol/L), hyperfermentemia – increased levels of AST (103.4 U/L) and ALT (64.2 U/L), raised levels of creatinine (424.97mkmol/L) and urea (32.6 mmol/L), hypokalemia (3.1 mmol/L), hypoproteinemia (48.4 g/L); cardiac biomarkers were increased – CK-NAC 364.3 U/l, CK-MB 68.83 U/l.

ECG on admission: bradycardia, heart rate 40 bpm, junctional rhythm, LBBB (QRS 0.14 ms), acute circular MI (ST elevation > 2 mm III, AVF, V1-V5, ST depression 1 mm I, AVL).

Transthoracic echocardiogram data: Signs of total heart failure with hypertrophy and dilation of heart chambers, valvular regurgitation, LV contractility reduction. Development of pulmonary hypertension. Hydropericardium. Hypokinesia of the LV posterior wall, which is affected by infarction.

Data of the abdomen ultrasound: diffuse alteration of liver and pancreatic parenchyma; hepatomegaly; venous liver congestion; bilateral hydrothorax.

CLINICAL DIAGNOSIS

Main disease

Coronary artery disease. Acute repeated ST elevated circular myocardial infarction (28.08.2015). Postinfarction inferior wall cardiosclerosis (2006). Killip IV.

Essential hypertension III stage, 2 grade.

Persistent atrial fibrillation, tachysystolic form.

Risk score 4 (very high).

Chronic congestive heart failure II NYHA with the reduction of LV contractility.

Complication

Junctional rhythm, bradycardia
Acute prerenal failure

Concomitant diagnosis

Alcoholic liver disease
Obesity class I

COURSE OF DISEASE

On the third day of the disease early in the morning in arose complains such as black colored stools, fatigue, and dizziness.

During inspection: body T – 36,5° C, Pulse – 34 bpm, BP – 90/60 mm Hg, respiratory rate – 20 pm. Patient was drowsy and sluggish. Skin and mucous membranes were pale and dry.

Bronchial breath sounds of the lungs to auscultation. Decrease breath sounds in bases. Rhonchi and crackles were not auscultated. Pulse was regular, soft and small (pulsus filiformis). Soft S1 heart sound to auscultation. Abdomen was soft and tender in epigastric region. Hepatomegaly (+4 cm), palpation of liver was tender. The kidneys were not palpable.

Complete blood count revealed rapid significant decline level of RBC (2.39 10*12/L), Hb (76 g/L), and HCT (23.1 %); persisting neutrophilic leukocytosis (WBC 12.5 10*9/L, NE 9.5 10*9/L, 76.1 %).

Fibroscopy was carried out to the patient: several acute ulcers 0,5–0,8 cm in diameter, covered by fibrin were found in antrum of the stomach.

The same day in the evening in patient took place respiratory arrest and cardiac arrest: absence of the breathing and pulsation of the main arteries, pupil dilation, and loss of consciousness.

ECG-monitor: isoline.

In patient developed clinical death. Emergency measures: IV epinephrine, indirect cardiac massage. After 3 min, emergency measures were successful: cardiac activity and respiration were restored – PS 80 bpm, BP 150/100 mmHg, RR 18 per min.

In this case the most prominent atherosclerotic plaque was localized in the right coronary artery. The right coronary artery distributes blood to right ventricle, right atrium, posterior portion of the interventricular septum, posterior wall of the left ventricle and the heart conduction system (including sinoatrial node). Ischemia of SA node may lead to its dysfunction (bradycardia, SA arrest, etc.)

Considering the severity of the patient's condition, refractory bradycardia (HR 40 bpm), developed acute renal failure and GIT bleeding, clinical death, to improve patient's condition, temporal pacemaker was implanted.

Temporal pacemaker implantation improved organ perfusion: renal failure abated (creatinine 74.77 mkmol/L, urea 9.8 mmol/L), also occurred rising of total protein level (50.1 g/L) and rising level of potassium (5.0 mmol/L) to normal ranges.

Seven days after pacemaker implantation fever had been developed, body temperature was in ranges 37.7–38.2°C, also persist neutrophilic leukocytosis (WBC 10.0 10*9/L, NE 7.9 10*9/L, 79.7 %) and increased ESR (18 mm/h).

Transthoracic echocardiogram was repeated: development of bacterial vegetations on the right coronary cusp of aortic valve were revealed; signs of total heart failure with hypertrophy and dilation of heart chambers, valvular regurgitation, LV contractility reduction, pulmonary hypertension, hydropericardium, hypokinesia of the LV posterior wall were preserved.

Chest X-Ray was carried out: absence of pulmonary seeding, pulmonary congestion, bilateral hydrothorax, cardiomegaly.

Blood culture samples were negative.

FINAL DIAGNOSIS

Main disease

Coronary artery disease. Repeated ST elevated circular myocardial infarction (28.08.2015). Postinfarction inferior wall cardiosclerosis (2006). Killip IV

Essential hypertension III stage, 2 grade

Persistent atrial fibrillation, tachysystolic form

Chronic heart failure with systolic dysfunction of left ventricle

Risk score 4 (very high).

Complication

Junctional rhythm, bradycardia (40 bpm)

Acute prerenal failure

Clinical death

Temporal pacemaker implantation

Possible nasocomial active device-related (temporal pacemaker) infective endocarditis

Acute gastric stress ulcers, GIT bleeding

Anemia of blood loss, moderate

Concomitant diagnosis

Alcoholic liver disease, alcoholic hepatitis

Obesity class I

MANAGEMENT

1. Life style modification: diet: low in saturated fat and high in omega-3 fat, low carbohydrates, low sodium (3g/d); limit alcohol consumption; body weight control: goal BMI 18.5–24.99; smoking cessation.

2. Acute coronary syndrome treatment: IV Morphine sulfate; low molecular weight heparin (enoxaparin 80 mg/2d); aspirin 75 mg/d; clopidogrel 75 mg/d; atorvastatin 80 mg/d; eplerenonum 25 mg/d; ramipril 2,5 mg/d; pantoprazole 40 mg/d [4].

Additional recommendations: thrombolytic therapy (IV alteplase) or PCI [5].

3. Bradycardia treatment: atropine IV/IM; temporal pacemaker implantation [6].

Recommendations: pacemaker implantation change to transcutaneous pacing to avoid infective endocarditis development [7].

4. Infective endocarditis treatment: pacemaker removal; IV Cefepime 1,0 g 2 times/d 14 days; IV Vancomycin 2 g 1 times/d 7 days [8].

5. Acute renal failure treatment: reduction of cardiac output due to myocardial infarction and bradycardia due to sinoatrial ischemia, hypovolemia due to GI bleeding lead to prerenal acute kidney injury. Temporal pacemaker implantation improves cardiac output and kidney perfusion. IV solutions to increase blood volume are not indicated, because of increasing heart preload and heart demands [9–10].

6. GIT bleeding treatment: withhold of low molecular weight heparin, aspirin, and clopidogrel. Prescribe: hemostatic therapy (IV ε-aminocapronic acid 100,0 2 times/d, IV etamsilate 12,5 % 4,0 3 times/d, IV menadione 1 % 1,0 3 times/d); antisecretory drugs (IV famotidine 20mg 2 times/d, IV pantoprazole 40 mg 1 time/d) [11].

7. Anemia treatment: diet (red meat, beetroot, spinach, pomegranates, soy beans, whole grain bread, peaches, prunes and raisins); ferrous sulfate 60 mg/d per os for 3 months; folic acid 400 mcg/day per os for 3 months [12].

8. Alcoholic liver disease treatment: Essential phospholipids 300 mg/ 2d for 3 months; Argininum 1.5 g/ 2d for 3 months.

CONCLUSIONS

The case report demonstrates complicated myocardial infarction, and reminds clinicians that prompt recognition and management are critical in this uncommon grave clinical case. Clinicians must keep potentially lethal complications in mind when evaluating these unstable patients. Early, aggressive, and judicious treatment of these complications may substantially decrease the morbidity and mortality associated with acute myocardial infarction.

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HYPERTROPHIC CARDIOMYOPATHY IN MULTIMORBIDITY

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Aspects of diagnosis, difficulties in the diagnosis and optimal therapeutic strategies in patient with hypertrophic cardiomyopathy and comorbid conditions such as arterial hypertension, ischemic heart disease, dyslipidemia, diabetes mellitus type 2, stenosis of the left renal artery, obesity are reviewed on the example of clinical case. Hypertrophic cardiomyopathy combined with multimorbidity conditions requires a high-quality medical management, where the main goal is to improve the quality and duration of patient's life. This goal is being achieved by optimizing patient's lifestyle and assigning only the minimum amount of medications. Necessity of careful diagnosis of hypertrophic cardiomyopathy, evaluation of the risk of sudden death and search of optimal treatment in patients with multimorbidity pathology are demonstrated in clinical case.

KEY WORDS: hypertrophic cardiomyopathy, multimorbidity, diagnosis, rational pharmacotherapy, quality of life, disease prevention

ГІПЕРТРОФІЧНА КАРДІОМІОПАТІЯ В МУЛЬТІМОРБІДНОСТІ

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На прикладі клінічного випадку розглядаються аспекти діагностики, складності в постановці діагнозу та оптимальна лікувальна тактика у пацієнта із гіпертрофічною кардіоміопатією та супутніми захворюваннями, такими як артеріальна гіпертензія, ішемічна хвороба серця, дисліпідемія, цукровий діабет 2 типу, стеноз лівої ниркової артерії, ожиріння. Гіпертрофічна кардіоміопатія в сукупності з мультіморбідними станами вимагає якісного медичного менеджменту, в якому головна ціль - підвищення якості та тривалості життя пацієнта досягається оптимізацією способу життя та призначенням мінімуму ефективних лікарських препаратів. Клінічний випадок демонструє необхідність ретельної діагностики гіпертрофічної кардіоміопатії, оцінки ризику раптової смерті та пошуку оптимального лікування при мультиморбідних станах.

КЛЮЧОВІ СЛОВА: гіпертрофічна кардіоміопатія, мультиморбідність, діагностика, раціональна фармакотерапія, якість життя**,** профілактика

ГИПЕРТРОФИЧЕСКАЯ КАРДИОМИОПАТИЯ В МУЛЬТИМОРБИДНОСТИ

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На примере клинического случая рассматривается аспекты диагностики, сложности в постановке диагноза и оптимальная лечебная тактика у пациента с гипертрофической кардиомиопатией и сопутствующими заболеваниями, такими как артериальная гипертензия, ишемическая болезнь сердца, дислипидемия, сахарный диабет 2 типа, стеноз левой почечной артерии, ожирение. Гипертрофическая кардиомиопатия в совокупности с мультиморбидными состояниями требует качественного медицинского менеджмента, в котором главная цель - повышение качества и продолжительности жизни пациента достигается оптимизацией способа жизни и назначением минимума эффективных лекарственных препаратов. Клинический случай демонстрирует необходимость тщательной диагностики гипертрофической кардиомиопатии, оценки риска внезапной смерти и поиска оптимального лечения при мультиморбидных состояниях.

КЛЮЧЕВЫЕ СЛОВА: полиморбидность, полипрагмазия, рациональная фармакотерапия, качество жизни, профилактика

INTRODUCTION

Semi-centennial history of the study of the problem of hypertrophic cardiomyopathy (HCM) reflects the evolution of knowledge in the field of etiology, pathogenesis and clinical course, treatment options of this disease, diagnosis and prognosis.

Hypertrophic cardiomyopathy (HCM) is an autosomal dominant genetic disorder characterized by massive (over 1,5 cm) left ventricular hypertrophy (LVH), and/or in rare cases, the right ventricle, the most commonly observed pattern is asymmetrical thickening of the anterior interventricular septum (IVS). These features can cause dynamic obstruction of the left ventricular outflow tract, diastolic dysfunction, myocardial ischemia, and an increased risk of developing severe, life-threatening supraventricular and ventricular tachyarrhythmia and sudden death [1–2].

Multimorbidity is the combination of multiple chronic or acute diseases and medical conditions in one person. Multimorbidity is the hallmark of an older age, it individualizes clinical picture of HCM, and requires an adequate diagnostic and therapeutic strategies [3–4].

Medical management of such patients with multimorbidity in the cardiology clinic has not been studied enough, which is shown in the given clinical case.

CLINICAL CASE

Male patient, 59 years old, electrician, resident of urban area.

COMPLAINTS

Recurrent headaches of compressive nature in the occipital region, going away after an intake 1 tablet of aspirin within 15 minutes. Fluctuations in blood pressure (BP) measurement at home with a maximum BP 160–170/100 mm Hg; shortness of breath of mixed character, during the walk or excessive physical effort (lift to the 5th floor), disappears within 10 minutes after the rest.

ANAMNESIS MORBI

2004: Arterial hypertension (AH) with a maximum BP 180/100 mmHg. He is constantly taking valsartan 80 mg.

15.02.16: Patient was treated in the outpatient department by administrative district due to the crisis of AH.

18.02.16: He was admitted to the hospital by administrative district for examination and treatment.

In a hospital on an ECG revealed hypertrophy with marked congestion and subendocardial changes on anterior and septum area of LV.

On Echocardiography: severe hypertrophy of IVS, subaortic stenosis?

Diagnosis: Hypertrophic obstructive cardiomyopathy. Secondary arterial hypertension stage II. Mitral valve insufficiency stage I. Atherosclerosis of major cerebral arteries. 1st stage of heart failure, 2nd functional class with preserved systolic function (EF 50 %). Diabetes mellitus type 2, moderate severity. Misc (hypertensive, diabetic) nephropathy.

Drug therapy (Isosorbide dinitrate intravenous, acetylsalicylic acid + magnesium hydroxide, Olmesartan medoxomil, Amlodipine, Bisoprolol, Rosuvastatin) was effective.

22.03.16: Patient was sent to Kharkiv Railway Clinical Hospital № 1 of Brence of «HC» JSC «Ukrzaliznytsia» for the examination and diagnosis verification in the cardiology department.

ANAMNESIS VITAE

Patient has satisfactory living conditions. He eats regularly and varied.

Industrial hazards are being denied.

Patient experiences acute respiratory infections (3–4 times a year), measles.

From 2008 – diabetes mellitus type 2 (takes Metformin 1000 mg). Patient conducts daily measurement of glucose level.

Surgeries: removal of a lipoma in the right scapula (2012).

Patient denies viral hepatitis, tuberculosis, sexually transmitted diseases. Allergic anamnesis is not burdened.

Hereditary history burdened by hypertension on father's side (who died of a stroke at age 61).

OBJECTIVE EXAMINATION

Patient's condition is satisfactory. He is active, but emotionally labile. Height – 162 cm, weight – 82 kg, body mass index (BMI) = 31,2 kg/m2. Skin has pale pink

color. Peripheral lymph nodes: submandibular, axillary and inguinal lymph nodes soft consistency, painless, moderately agile and not soldered to each other and the skin. Lobes of the thyroid gland are not palpable; the isthmus is palpated in the form of a uniform cross-strand smooth, 1 cm wide.

There is a mild lung sound above lungs, vesicular breathing in auscultation. Border of the heart expanded to the left. Activity of the heart is rhythmic; heart rate (HR) 75 beats/min. Heart sounds are muffled. Diffuse systolic murmur, with its epicenter in the apex. BP is 150/80 mm/Hg on hypotensive therapy.

Abdomen is enlarged, painless on palpation. Liver sticks out below the rib cage for about 1–1.5 cm, painless.

Pasternatsky's symptom is negative on both sides. Physiological functions: normal. No swelling.

LABORATORY AND INSTRUMENTAL TESTS

Complete blood count (CBC): figures are in the normal ranges.

Urinalysis: glycosuria (10.9 mmol/l).

Biochemical analysis of blood: high level of glucose (16.24 mmol/l) and glycated hemoglobin (10 %)

Analysis of lipid: increased levels of very low density lipoprotein (1.48 mmol/l), triglyceride level (3.3 mmol/l) and atherogenic index (3.91 mmol/l) – Familial hypertriglyceridemia type IV.

ECG showed sinus rhythm, regular. Heart rate 78 beats/min. Severe left ventricular hypertrophy. Pathologic Q in V1–V3 with ST segment elevation in V3. T-wave inversion in I, aVL, V5, V6.

According to the ultrasound of the heart from 23.02.2016: Severe hypertrophy of the IVS, mitral valve insufficiency of I degree, hypokinesia of IVS, hypertrophic cardiomyopathy, subaortic stenosis. Left ventricular injection fraction – 50 %.

According to the ultrasound of the heart from 23.03.2016: Severe left ventricular hypertrophy, concentric type, sclerotic changes of the aortic wall, fibrosis and calcification of the aortic and mitral valves , signs of increased diastolic stiffness of the left ventricle walls, mitral regurgitation I stage, tricuspid regurgitation I stage. Left ventricular injection fraction – 65 %.

According to the ultrasound of the heart from 30.03.2016: Left ventricular hypertrophy with an asymmetrical thickening of the anterior septal and anterior- lateral segments with mild left ventricular outflow tract obstruction (systolic PGmax=7 mm Hg at rest, systolic PGmax=21 mm Hg at the height of Valsalva's test). Dilatation of left atria. Sclerotic changes of the aortic wall. Pulmonary hypertension (systolic P = 31 mm Hg).

Coronary angiography (CA): right type of coronary blood supply. 80 % extended occlusion of the anterior descending artery and 30 % occlusion of the right coronary artery.

5-hour ECG monitoring by Holter: Rhythm is sinus with an average heart rate during the day 76 beats/min, the maximum is 96 beats/min. Ischemic changes were not detected. Single ventricular and supra-ventricular extrasystoles.

Treadmill test: The test is positive. Tolerance to physical load 10.6 MET. Submaximal heart rate was not achieved. On the ECG recorded ST elevation in leads V4 from baseline to 2.5 mm, V5 from baseline to 2.0 mm, V6 – to 1.5 mm in physical load 10.6 MET. Any cardiac complaints the patient did not show for the entire study period. The recovery period was without features. Completed load corresponds to the I F.C. of angina.

The test with 6-minute walk: The test result complies with functional class II chronic heart failure (distance – 400 m).

Ultrasound of abdominal and retro-abdominal organs: diffuse changes of liver and pancreas parenchyma without magnification. Hepatomegaly. Microcal-culosis of kidneys. Cysts of both kidneys.

Consultation of ophthalmologist: Angiopathy of the retina of 2 degrees.

Consultation MD., Professor of cardiology and functional diagnostics of KhMAPE: Patient has HCM, obstructive form, hypertrophy of the Antero-septal and Antero – lateral parts of 2-st. Dilatation of the left atrium. Signs of pulmonary hypertension. Arterial hypertensive stage II, 2 degree, very high cardiovascular risk, 1st stage of heart failure, 2nd functional class with preserved systolic function Comorbid conditions: diabetes mellitus type 2, non-compensated.

Given the presence of diabetes, signs of renal arteries shown holding coronary angiography for the assessment of coronary artery.

Recommend tests: Ultrasound of renal arteries with Doppler – Effect, genetic research (Class I evidence) [1], consultation of endocrinologist.

DIAGNOSIS

The underlying disease: Hypertrophic cardiomyopathy with obstruction of the outflow tract of 1 degree, hypertrophy of the Antero-septal and Antero – lateral parts of 2 degree. Dilatation of the left atrium. Pulmonary hypertension 1 degree. Secondary arterial hypertensive stage II, 2 degree, high additional risk. Coronary heart disease: Silent Myocardial Ischemia**.** Coronary angiography (04.04.16): 80 % occlusion of the anterior descending artery and 30 % occlusion of the right coronary artery. Extrasystolic (supraventricular and ventricular) arrhythmias. Dyslipidemia type IV. Familial hypertriglyceridemia. Insufficiency of the mitral valve of 1 degree. IIa stage of heart failure, 2nd functional class with preserved systolic function (EF=65 %).

Comorbid conditions: Diabetes mellitus type 2, medium- hard course, decom-pensation. Obesity 1 degree. Chronic kidney disease stage 0. Microurolitiasis. Moderate stenosis of the left renal artery. Cysts of both kidneys.

TREATMENT RECEIVED IN HOSPITAL (domiciliary)

Isosorbide dinitrate – 0.01 % intravenosus, Acetylsalicylic acid/ Magnesium hydroxide – 75 mg, Olmesartan medoxomil – 20 mg, Amlodipine – 10 mg, Bisoprolol – 2.5 mg, Rosuvastatin – 10 mg, Metformin – 1000 mg, Glimepirid – 2 mg.

RECOMMENDATIONS

1. Lifestyle modification: lipid-lowering diet with restriction of refined carbohydrates, increase of the intake of vegetables and fruits, restriction of consumption of table salt, water consumption amounts at the rate of 20 mL/kg in the winter and up to 30 mL/kg in the summer under the control of body weight; limit excessive exercise, allowed fresh air, swimming [5–6].

2. Drug therapy: Nebivolol is 5 mg in the morning (under the control of heart rate and blood pressure), Lisinopril – 10 mg in the evening, Acetylsalicylic acid – 100 mg 1 time per day, Rosuvastatin 10 mg 1 time per day for a long time, Metformin – 1000 mg, Glimepirid – 2 mg [7–12].

CONCLUSIONS

Hypertrophic cardiomyopathy in older age may be associated and combined with other diseases.

In this clinical case, it was combined with arterial hypertension, ischemic heart disease, dyslipidemia, diabetes mellitus, stenosis of the left renal artery, obesity. This combination requires a high-quality of medical management in which the goal of improving the quality and duration of life of the patient is achieved by modification of lifestyle and the minimum medical assignments when polypharmacy is not permitted [13–14].

However, in this clinical case, to confirm the diagnosis of hypertrophic cardiomyopathy, genetic testing is needed.

Thus, the strategy of therapeutic interventions in HCM is complex and involves an individual analysis of the complex of clinical, anamnestic, hemodynamic variables, as well as results of genetic diagnosis, assessment of risk of sudden death, characteristics of the disease, and effectiveness of treatment options.

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CLINICAL CASE OF INFECTIVE ENDOCARDITIS IN IV DRUG ABUSER

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Infective endocarditis in intravenous drug abuser is reviewed on the example of clinical case. Clinical examination, the clinical diagnosis, recommendations for surgical treatment, choice of optimal therapy are outlined in patient with infective endocarditis. The features of infective endocarditis in IV drug abused patients were studied.

KEY WORDS: infective endocarditis, drug abuser, pharmacotherapy, treatment, disease prevention

КЛІНІЧНИЙ ВИПАДОК ІНФЕКЦІЙНОГО ЕНДОКАРДИТУ У НАРКОМАНА

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Інфекційний ендокардит у внутрішньовенного наркомана розглядається на прикладі клінічного випадку. Клінічне обстеження, клінічний діагноз, рекомендації з оперативного лікування, вибір оптимальної терапії описані у пацієнта з інфекційним ендокардитом. Вивчені особливості течії інфекційного ендокардиту у внутрішньовенних наркоманів.

КЛЮЧОВІ СЛОВА: інфекційний ендокардит, зловживання наркотиками, фармакотерапія, лікування, профілактика захворювання

КЛИНИЧЕСКИЙ СЛУЧАЙ ИНФЕКЦИОННОГО ЭНДОКАРДИТА У НАРКОМАНА

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Инфекционный эндокардит у внутривенного наркомана рассматривается на примере клинического случая. Клиническое обследование, клинический диагноз, рекомендации по оперативному лечению, выбор оптимальной терапии описаны у пациента с инфекционным эндокардитом. Изучены особенности течения инфекционного эндокардита у внутривенных наркоманов.

КЛЮЧЕВЫЕ СЛОВА: инфекционный эндокардит, злоупотребление наркотиками, фармакотерапия, лечение, профилактика заболевания

INTRODUCTION

Infective endocarditis (IE) – defined as an infection of the endocardial surface of the heart, which may include one or more heart valves, the mural endocardium, or a septal defect. IE still remains a diagnostic challenge because of its diverse nature and evolving epidemiological profile. The clinical picture of IE differs much depending on causative microorganism, pre-existing cardiac disease, the presence or absence of prosthetic valves or cardiac devices have their influence too. Because of that, diagnosis IE should be suspected in different clinical situations [1].

Between all cases of IE, right-sided disease accounts about 5–10 %. Right-sided EI is the most frequent for intravenous drug abusers (IVDAs), especially in patients with concomitant human immunodeficiency virus or in immunosuppressed patients [2, 3]. In case of IE of the right heart side, the tricuspid valve will be an affected part of the valvular system, but other valves may be infected too [4]. Right-sided IE in IVDA patients with tricuspid valve vegetations greater than 2 cm in diameter [5] and present acute respiratory distress syndrome [6] usually have higher mortality than the same patients with involvement in the pathological process other heart parts. The most appropriate

theory of IE development in IVDA is based on understanding that caused by bacterial «bombardment» endothelial damage of the tricuspid valve [6]. The usual clinical sings and symptoms of right-sided IE are persistent fever, bacteraemia and multiple septic pulmonary emboli, which may onset as chest pain with cough or haemoptysis. When systemic emboli happens, paradoxical embolism or associated left-sided IE should be suspected. Despite its rare frequency, isolated right HF can be caused by pulmonary hypertension or severe right-sided valvular regurgitation [4]. Tricuspid IE usually easy to observe because of the anterior position of this valve and large vegetations in diameter nature [7].

CLINICAL CASE

Man, 24 years old, unemployed, resident of urban area.

COMPLAINTS

Patient was admitted to the hospital with complains on dyspnea, impossibility of deep inhale, increasing of body temperature above 38°C, palpitation, edemas of low extremities, icteric skin color.

ANAMNESIS MORBI

05 – September – 2015 was delivered by ambulance in the therapy department after infectious diseases specialist consultation with diagnosis: Community – acquired 2-sided pneumonia. Chronic toxic hepatitis. Secondary enteropathy. Sepsis?

10 days before admission patient felt bad, first time was appeared high body temperature till 39 °C, yellowish color of skin, palpitation. Ambulance was called, didn't visit local family doctor.

Previously was drug addict (IV drugs injections).

ANAMNESIS VITAE

Patient lives with mother and brother in an isolated apartment. He eats irregularly, does not follow any diet.

Childhood infections, injuries, tuberculosis, sexually transmitted diseases were denied by patient. Hereditary diseases are not identified. Allergic history is not burdened.

Smoker during 5 years, do not abuse alcohol.

2013 – appendectomy.

OBJECTIVE EXAMINATION

Patient's condition is severe, conciseness - clear, body position - lying on his back. Patient can orientate himself in place, time, his personality. Yellowish skin and mucosae, herpes labialis. Lobes of the thyroid gland are not palpable, the isthmus is palpated in the form of a uniform cross-strand smooth, 0.5 cm wide. Musculoskeletal system – no pathological changes. BR – 24–26/min, Sp O2 – 91–92 %. There was found a dullness below scapula angles from both sides during percussion, weak breathing, whizzing in upper parts, crepitation – lower parts 2-sided in auscultation. Activity of the heart was rhythmic, 120 bts/min. Borders of the heart: right border – outside of midsternal right line on 2cm. Heart sounds were rhythmic, muffled, systolic murmur in IV point of auscultaion. BP 80/40 mm Hg. Abdomen: normal size, symmetric, pain during palpation in right hypochondrium. Liver margin was 3 cm below right rib cage, painless. The spleen palpated 1 cm below the left costal arch. Pasternatsky's symptom is negative on both sides. Physiological functions: liquid stool, 2–3 times, dark color. Edemas of calves and feet. Varicose vein disease of lower extremities – absent.

Patients temperature ranges in time of treatment in hospital wars indicated in pic. 1.

LABORATORY AND INSTRUMENTAL TESTS

Complete blood count (CBC) from 05-sep-2015: hypochromic anemia I stage (Hemoglobin (Hb) – 110 g/l, red blood cells (RBC) – $3.6*10^{12}$/l), leukocytosis (white blood cells (WBC) – $12*10^{9}$/l) and Erythrocytes sedimentation rate (ESR) – 15 mm/h.

Complete blood count (CBC) from 22-sep-2015: hypochromic anemia III stage (Hb– 37 g/l, RBC – $1.4*10^{12}$/l, color index – 0.79, poikilocytosis), ESR – 82 mm/h.

Complete blood count (CBC) from 22-sep-2015 after blood transfusion: hypochromic anemia III stage (Hb– 53 g/l, RBC – $2.3*10^{12}$/l, color index – 0.79, microcytosis, poikilocytosis), ESR – 65 mm/h.

Urinalysis: proteinuria – 0.216 g/l, leukocyturea – 25–30 in the field, hyaline and granular casts – several.

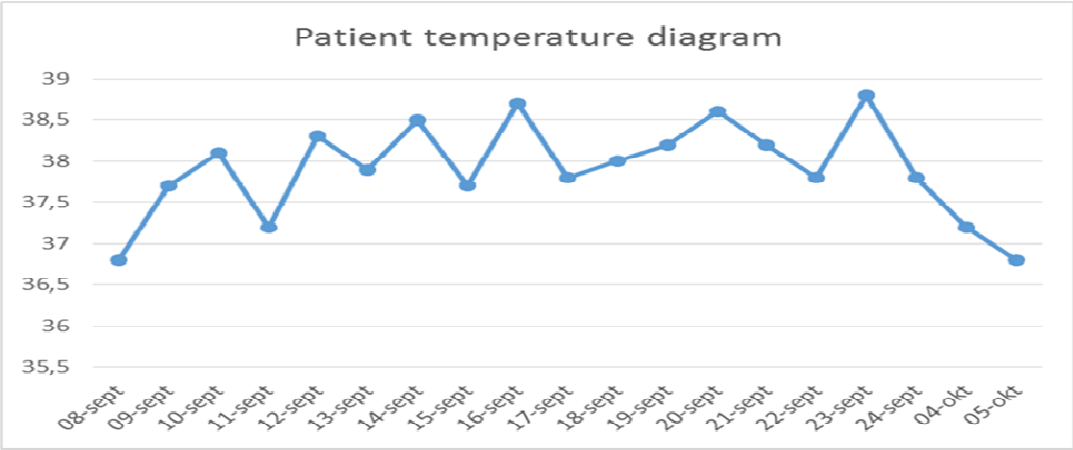
Cardiac markers: CK-MB – in the normal range.

Liver function test: bilirubin was increased – 25 mmol/l, AST level was increased – 63U/l, ALT level was increased – 52U/l. Positive marker for viral hepatitis C were found: Anti-HCV – 0.712.

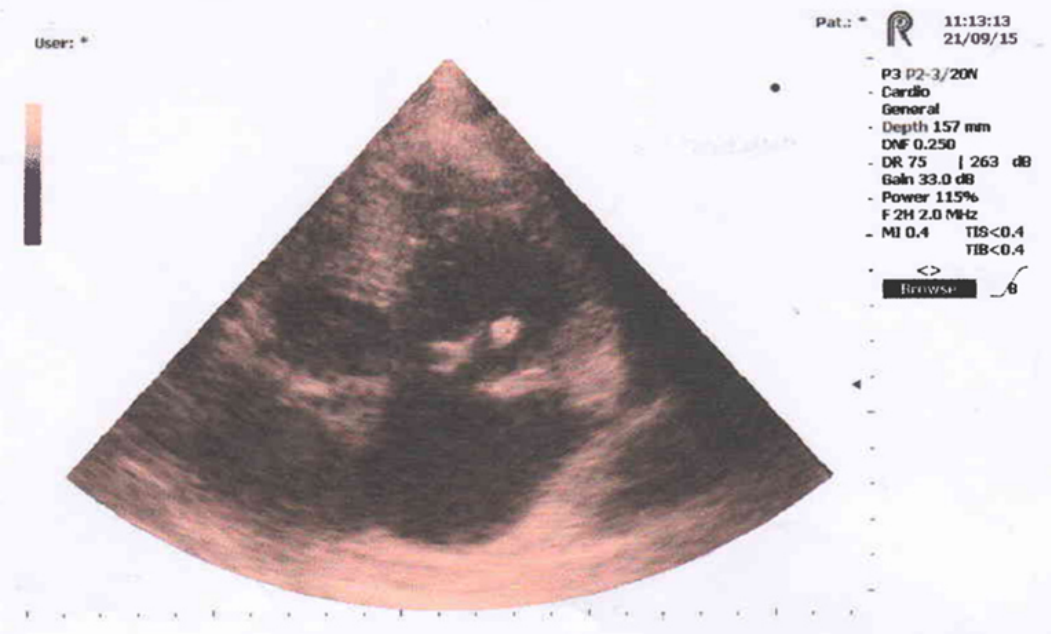
ECG showed sinus tachycardia, regular, heart rate – 95 bts/min.

Chest X-ray: In the middle and lower parts of left lung can be seen transparency decreasing due to infiltration. Right lung – in the middle region can be seen focal areas of infiltration. Diaphragm's cupulas are flattened. Sinuses are poorly differentiated. Flat waist of heart. Right heart border is increased. Elongation of aorta. Conclusion: 2-sided pneumonia.

Echocardiography: EF (ejection fraction) – 60 %. Dilatation of the right heart chambers. Infective endocarditis with involvement of tricuspid valve (on anterior leaflet of tricuspid valve is present a high density vegetation on narrow base – 14 mm. On septal leaflets – 6 mm high density vegetation on wide basement). Tricuspid regurgitation 3rd degree (see pic. 2)



Pic.1 Temperature of the patient while staying in the hospital



Pic. 2 Echocardiography from 11-sep-2015

Ultrasound of kidneys: Right sided nephroptosis. 2-sided hydrocalicosis.

Blood culture was taken 2 times: 12-sep-2015 and 27-sep-2015, but both times it was negative.

Echocardiography was made again in V. T. Zaycev Institution of general and urgent surgery NAMS of Ukraine: EF – 68 %. No akinesia zones. Multiple vegetation's on tricuspid valve. Tricuspid regurgitation 3rd degree. Dilatation of the right heart chambers. Hypertrophy of left ventricle.

Consultation of the cardiac surgeon in V. T. Zaycev Institution of general and urgent surgery NAMS of Ukraine: Acute infectious endocarditis of IV drug users, culture – negative, right – sided, primary affection of tricuspid valve, was recommended to continue antibacterial treatment, routine surgical intervention in V. T. Zaycev Institution of general and urgent surgery NAMS of Ukraine.

DIAGNOSIS

In clinical practice the diagnosis of IE usually relies on the association between an infective syndrome and recent endocardial involvement. Diagnosis of infective endocarditis in our patient clinical case is definitive, because according to modified Duke criteria of infective endocarditis [1], patient had: 1 major (pathological legions; vegetations or intracardiac abscess) and 3 minor criteria (patient is intravenous drug user; temperature was below 38 °C; echocardiographic findings consisted with endocarditis, but not vegetations – dilation of right chambers, new tricuspid valve regurgitation IIIrd degree).

The underlying disease: Acute right-side infectious native-valve endocarditis of IV drug users, culture – negative, right – sided, primary affection of tricuspid valve, target organs (heart, lungs).

Complications: Congestive Heart Failure with preserved left ventricular pump function (ejection fraction = 60 %), III C functional class by NYHA. Community-acquired 2-sided pneumonia, moderate. RF II stage. Hypo-chromic anemia 3rd stage.

Comorbid conditions: Chronic C hepatitis with minimal activity.

TREATMENT RECEIVED IN HOSPITAL

Antibacterial treatment: levofloxacin 500mg IV 1 time/day from 05/09 till 15/09/15, amoxicillin/clavulonic acid IV 1000 mg 2 times/day from 05/09 till 13/10/15, vancomycin 1gr IV 2 times/day from 14/09 till 30/09/15 (patient cannot continue therapy due to financial problems), gentamycin 80 mg 2 times/day IM from 19/09 till 13/10/15, «Biseptol» 480 mg 2 tabl 3 times/day from 22/09 till 13/10/15, levomicetin 1 gr 4 times/day IV from 02/10 till 13/10/15.

Other drugs prescripted: dexamethasone 8 mg IV in 200 ml of 5 % dextrose solution #3, trifas 20 mg IV 1 time/day then 10 mg/day orally, ampril 2.5 mg / day, bisoprolol 5 mg 1 time/day, «Glutargin» 1 tabl 3 times/day from 14/09 till 13/10/15, vicasol 1.0 ml IM 5 days, aminocapronic acid 100 ml IV #1.

Blood transfusion (erythrocytes mass) 333 ml gr IV (RH+) IV 24/09/15.

RECOMMENDATIONS

1. Heart failure (HF) is the most frequent complication of IE and represents the most common indication for surgery in IE. The presence of HF is an indication for early surgery in native – valve endocarditis (NVE) and rostatic- valve endocarditis (PVE), even in patients with cardiogenic shock. [1]. Patient was referred to V. T. Zaycev Institution of general and urgent surgery NAMS of Ukraine for planned surgery, but because of financial problems and asocial life-style patient refused, surgery intervention wasn't made). Drug therapy: bisoprolol 5 mg 1 time/day, ampril 2.5 mg / day, spironolactone 25 mg/day.

2. Despite the recommendations of general surgery rejection in patients with right-sided IE [1], for our patient surgical intervention should be recommended because of presence of right HF secondary to severe tricuspid regurgitation and IE caused by organisms that are difficult to eradicate despite adequate antimicrobial therapy (temperature curve on pic. 2).

3. Embolic events are a frequent and life-threatening complication of IE related to the migration of cardiac vegetations [1]. Age, diabetes, atrial fibrillation, previous embolism, vegetation length and S. aureus infection were associated with an increased embolic risk in patient with IE and were used to create an 'embolic risk calculator' [8]. The highest risk of embolism patient with IE usually has during the first 2 weeks of antibiotic therapy, during this period benefits of surgery to prevent embolism are greatest [1]. Patient was prescribed clopidogrel – 75 mg 1 time a day continuously.

CONCLUSIONS

There were no significant changes in clinical and microbiologic picture of IE in IVDA during years. As usually, the most frequent area of infection in this type of patients is the tricuspid valve, the disease prognosis is relatively good and S. aureus is the main etiologic agent. In regard that patients with a history of IE are at risk of recurrent infection, must be very strictly developed and introduced in practice re-infection preventive measures. At discharge, patients should be informed and clearly explained about all signs and symptoms of IE, to help them be aware of possible repeated episode of IE. Patient should understand, that in case of appearance a new fever or chills, or other infection's signs, appropriate testing, including microbiological ones before antibacterial treatment prescription should be requested.

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THE IMPORTANCE OF TIMELY TREATMENT OF THE CAUSES OF HEART FAILURE ON THE EXAMPLE OF THE CLINICAL CASE

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Acquired heart disease complicated by chronic heart failure (CHF), which significantly impairs the quality of life of patients and worsens the prognosis and remains radical surgical treatment with implantation of prosthetic valve. On the example of a clinical case are shown and discussed the results of a late replacement of the mitral valve in patient with acquired heart defect.

KEY WORDS: prosthetic valve, heart failure, acquired heart defect

ВАЖЛИВІСТЬ СВОЄЧАСНОГО ЛІКУВАННЯ ПРИЧИН СЕРЦЕВОЇ НЕДОСТАТНОСТІ НА ПРИКЛАДІ КЛІНІЧНОГО ВИПАДКУ

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Набуті вади серця ускладнюються хронічною серцевою недостатністю (ХСН), яка значно порушує якість життя пацієнтів та погіршує прогноз. Радиальним залишається хірургічне лікування з імплантацією штучних клапанів.

На прикладі клінічного випадку демонструються та обговорюються результати пізньої заміни мітрального клапану у пацієнтки з набутою вадою серця.

КЛЮЧОВІ СЛОВА: протезування клапану, серцева недостатність, набута вада серця

ВАЖНОСТЬ СВОЕВРЕМЕННОГО ЛЕЧЕНИЯ ПРИЧИН СЕРДЕЧНОЙ НЕДОСТАТОЧНОСТИ НА ПРИМЕРЕ КЛИНИЧЕСКОГО СЛУЧАЯ

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Приобретенные пороки сердца осложняются хронической сердечной недостаточностью (ХСН), которая значительно нарушает качество жизни пациентов и ухудшает прогноз. Радиальным остается хирургическое лечение с имплантацией искусственных клапанов.

На примере клинического случая демонстрируются и обсуждаются результаты поздней замены митрального клапана у пациентки с приобретенным пороком сердца.

КЛЮЧЕВЫЕ СЛОВА: протезирование клапана, сердечная недостаточность, приобретенный порок сердца

INTRODUCTION

Chronic heart failure (CHF) is an abnormality of cardiac structure or function leading to failure of the heart to deliver oxygen at a rate commensurate with the requirements of the metabolizing tissues, despite normal filling pressures (or only at the expense of increased filling pressures) [1]. Chronic heart failure (CHF) developing on the background of acquired heart defects can be cured only by surgery – a valve replacement.

Even in the event of a delay in seeking surgical treatment, this tactic is optimal for the stabilization stage heart failure and to prevent progression of the disease.

It`s much better to do replacement of valve later and prevent progression of CHF stage than not to do it at all [2].

The need for timely treatment, we demonstrated on the example of clinical case.

OUR PATIENT

70 years old woman, pensioner, worked as a salesman, city resident. Date of admission: 10 – October – 2015.

COMPLAINTS

Fatigue, dyspnea (paroxysmal nocturnal dyspnea (PND)), tachycardia, palpitation, nocturia, dizziness.

ANAMNESIS MORBI

These symptoms bother the patient more than 10 years. In 2012 complaints (symptoms) were worsened, because of this, the patient admitted to Institution of general and urgent surgery V. T. Zaycev NAMS of Ukraine. After lab-tests and instrumental examination the diagnosis was: Combined mitral valve disease with predominance of insufficiency.

Results of echocardiography before surgery (04.10.2012): Combined mitral valve disease with predominance of insufficiency (MV Hg 3+), S of MV = 2,8 cm^2. Dilatation of left atrium (4,3×5,2 mm) and left ventricle. Pulmonary hypertension (Hg 40 mm). EF = 77 %.

09.10.2012 the patient underwent mitral valve replacement with mechanical prosthesis St. Jude Medical № 27. The patient has taken all drugs that were prescripted after the surgery. This hospitalization is after increasing in data complaints.

ANAMNESIS VITAE

There was rheumatic fever attack in childhood. She had felt pain in the joins of lower extremities and got a temperature after sore throat. She don't remember which treatment had got. Heart murmur had detected in the survey in adulthood. Other infections, injuries, tuberculosis, sexually transmitted diseases were denied. Hereditary diseases are not identified. Allergological history is not burdened.

OBJECTIVE STATUS

General condition-moderate grave, Conciseness – clear, posture – active, body position – sitting on the chair. Patient can orientate herself in place, time, her personality. Height – 158 sm, weight – 63 kg, BMI – 25,2. Skin and mucosae are pale pink, with redness on the nose. Thyroid: no pathological changes. Skeleto–muscular system – deformity of the chest after sternotomy. BR – 22–24/min. Lung percussion: intermediate below scapula angles from both sides. Lung auscultation: decreased vesicular breathing, wheezes inferior parts both sides. Borders of the heart: left border – outside of midclavicular left line on 2 cm. Heart auscultation: rhythmic, heart tones – muffled, tone of mechanical valve, accentuated S2 over pulmonary artery. Pulse – rhythmic, 64 bits/min, BP 100/70 mm Hg. Abdomen: normal size, symmetric. Liver: liver margin is 1,5 cm below right rib cage. Spleen: normal. Pasternatsky symptom – negative from both sides. Edemas: absent. Varicose vein disease of lower extremities – absent. Stool: normal, everyday, dark color.

PLAN OF SURVEY IN THE HOSPITAL

Clinical blood test (CBT) and urine analysis, kidneys and liver function tests, electrolytes, lipid profile, INR – international normalized ratio, rheumatic factor, antistreptolysin O, electrocardiography(ECG), chest X-ray, echo-cardiography with Doppler.

RESULTS

Clinical blood test: Normal BC.

Urine analysis: Normal urine test.

Biochemistry test: The increased creatinine and decreased glomerular filtration rate (CKD-EPI GFR) that complies with chronic kidney failure stage 3.

Lipid profile: Hypercholesterolemia IIa type.

Electrocardiography: Regular sinus rhythm with heart rate 59/min. Deviation of electric axis to the left. Left ventricular hypertrophy.

Chest x-ray: Hypoventilation of the lungs. Pulmonary congestion. Pulmonary hyper-tension.

Heart ultrasound: Status after mitral valve replacement (prosthetic valve) (2012). The prosthesis is functioning correctly.

COMPLETE DIAGNOSIS OF OUR PATIENT

Mechanical prosthesis of mitral valve bileaflet type (09/10/2012) about combined mitral valve disease with predominance of insufficiency. Congestive heart failure with preserved left ventricular pump function (ejection fraction = 76 %), III C functional class by NYHA. Chronic kidney failure Stage 3. Atherosclerosis. Hyperlipidemia IIa type.

TREATMENT

Dietary sodium and fluid restrictions should be implemented in all patients with congestive heart failure. Limiting patients to 2 g/day of dietary sodium and 2 L/day of fluid will lessen congestion and decrease the need for diuretics.

Warfarin 5 mg 1 time/day, spironolactone 25 mg 1 time/day, ramipril 2.5 mg 1 time/day, bisoprolol 2.5 mg 1 time/day, torasemide 10 mg 1 time/day, atorvastatin 40 mg 1 time/day.

CONCLUSIONS

There is 3 years after surgical treatment of patients with replacement of the mitral valve there was stabilization of heart failure without signs of involution.

Clinical case shows that it is better later surgery, than not to do it at all. For creative development of CHF is required, however, as possible earlier intervention.

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CLINICAL CASE OF CHRONOTHERAPY OF ARTERIAL HYPERTENSION: FOCUS ON DIASTOLIC BLOOD PRESSURE

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A clinical case of chronotherapy of arterial hypertension (AH) with insufficient blood pressure (BP) night decline has described. Patient P., the BP daily means according to ambulatory BP monitoring (ABPM) was 148/84 mmHg, BP circadian rhythm violation with insufficient degree of nocturnal BP reduction. We recommended the patient to change the mode of antihypertensive drug intake from morning to evening in the same dose. After 3 months complete AH control was achieved with normalization of diastolic BP profile.

KEY WORDS: arterial hypertension, chronotherapy, ambulatory blood pressure monitoring, diastolic blood pressure

КЛІНИЧНИЙ ВИПАДОК ХРОНОТЕРАПІЇ ГІПЕРТОНІЧНОЇ ХВОРОБИ: ФОКУС НА ДІАСТОЛІЧНИЙ АРТЕРІАЛЬНИЙ ТИСК

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Описано випадок хронотерапії пацієнта з гіпертонічною хворобою (ГХ) з недостатнім ступенем нічного зниження артеріального тиску (АТ). Пацієнт П., середньодобовий АТ за даними добового моніторування АТ (ДМАД) 148/84 мм рт. ст., порушення циркадного ритму АТ за типом «недостатня ступінь нічного зниження АТ». Пацієнту рекомендовано змінити режим прийому гіпотензивного препарату в тій же дозі з ранкового на вечірній. Через 3 місяці було досягнуто повний контроль ГХ з нормалізацією добового профілю диастолічного АТ.

КЛЮЧОВІ СЛОВА: гіпертонічна хвороба, хронотерапія, добове моніторування артеріального тиску, диастолічний артеріальний тиск

КЛИНИЧЕСКИЙ СЛУЧАЙ ХРОНОТЕРАПИИ ГИПЕРТОНИЧЕСКОЙ БОЛЕЗНИ: ФОКУС НА ДИАСТОЛИЧЕСКОЕ АРТЕРИАЛЬНОЕ ДАВЛЕНИЕ

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Описан случай хронотерапии пациента с гипертонической болезнью (ГБ) с недостаточной степенью ночного снижения артериального давления (АД). Пациент П., среднесуточное АД по данным амбулаторного мониторирования 148/84 мм рт. ст., нарушение циркадного ритма АД по типу «недостаточная степень ночного снижения АД22». Пациенту рекомендовано сменить режим приема гипотензивного препарата в той же дозе с утреннего на вечерний. Через 3 месяца достигнут полный контроль ГБ с нормализацией суточного профиля диастолического АД.

КЛЮЧЕВЫЕ СЛОВА: гипертоническая болезнь, хронотерапия, суточное мониторирование артериального давления, диастолическое артериальное давление

INTRODUCTION

During ambulatory blood pressure (BP) monitoring (ABPM) its circadian fluctuations in accordance with international recommend-dations, are evaluated by the degree of its night-time reduction, the so-called «sleep-time relative BP decline» [1]. Depending on the value of this index the 4 types of circadian blood pressure profile are distinguished: «dippers» – physiological decrease in BP during the night – sleep-time relative BP decline 10–20 %; «overdippers» – an excessive fall in BP at night, sleep-time relative BP decline > 20 %; «non-dippers» – the lack of BP reduction at night, sleep-time relative BP

decline < 10 %; «night-peakers» – night-time BP more than during daily activity, sleep-time relative BP decline < 0 [1].

The cardiovascular risk (CVR) and AH prognosis in vast majority cases is assessed taking into account only the systolic BP (SBP) daily profile [2–3]. However, diastolic blood pressure (DBP) is an important predictor of AH outcomes and successful BP control [4] and its daily fluctuations may have clinical and prognostic significance in patients with hypertension also, that we has shown earlier [5].

A complete chronobiological analysis of BP using ABPM provides dynamic information about the BP level, which allows to optimize the drugs administration, taking into account the individual BP daily profile [6–7].

CLINICAL CASE

Patient P., male, 78 y.o., complained of chest pain, unstable BP with a tendency to increase. Chest pain occurs on physical exertion (climbing on the fifth floor), relived by rest or nitroglycerin. BP increases up to 175–180/90 – 100 mm Hg, usually in the evening, accompanied by palpitations, facial flushing and headache in the occipital region.

Retired engineer, does not smoke, no alcohol abuse. The living conditions are satisfactory. Physical activity is an average – daily perform morning exercises. Past medical history – chronic cholecystitis, pancreatitis, gastroduodenitis.

Patient has been suffering from arterial hypertension for 20 years. In 2011 a paroxysm of atrial flatter was revealed, with new-onset complete right bundle branch block. The same time chest pain occurred for the first time. Patient was examined in the institute of therapy named by L. T. Malaya, where the diagnosis was made: AH, II stage, 2 degree, high CVR. Ischemic heart disease, stable angina, II FC. Atherosclerotic cardiosclerosis. Paroxysmal atrial flatter. Heart failure, IIA stage, II FC. Since that time constantly takes losartan in a daily dose of 50 mg, once daily in the morning, occasionally – nitrogranulong, cardiomagnil, and nitroglycerin – as needed.

During last 2–3 months the chest pain frequency increased up to 3–4 times a week.

On physical examination, the general condition was satisfactory. Patient was of normal constitution, proper nutrition, height 1.72 m, weight 72 kg, BMI 24.3 kg/m2. Peripheral edema was not found. Over the entire surface of the lungs vesicular breathing has been auscultated, no wheezing. Cardiac activity was rhythmic with a heart rate of 70 beats/min. Cardiac sounds were clear, sonorous; accentuated 2 tone over the aorta. A short systolic murmur was determined in the aortic valve auscultating point. The borders of the relative cardiac dullness were not extended. BP on the right arm was 164/90 mm Hg, on the left arm – 165/88 mm Hg. Abdomen was soft, painless. The liver was at the edge of the costal arch, painless on palpation. Pasternatsky's sign was negative bilateral.

Further laboratory and instrumental investigations according to current standards [8–9] were prescribed, as well as ABPM and quality of life (QOL) survey using the SF-36 questionnaire was recommended.

The other obtained results: full blood count, urinalysis, fasting plasma glucose, creatinine, urea, blood electrolytes, ALT, AST, total cholesterol – within normal rangers; ECG – sinus rhythm, heart rate 65/min, complete right bundle branch block, frequent supraventricular extrasystoles; ultrasound of the heart – diffuse cardiosclerosis, moderate left ventricle hypertrophy, aortic stenosis 1st. with minimal regurgitation, EF – 59 %; ultrasound of the abdomen and kidneys – unremarkable. ABPM – the SBP and DBP daily means as well as hypertension load were increased – the stable systolic hypertension during all period of monitoring was recorded; the SBP, DBP, pulse pressure (PP) and mean arterial pressure (MAP) daily patterns were as non-dipper type (tab. 1–3.). The QOL survey showed low levels of physical and mental health components (tab. 4.).

Diagnosis: AH, stage II, grade 2, high CVR, violation of the SBP, DBP, MAP and PP circadian rhythm as non-dipper. Left ventricular hypertrophy. Ischemic heart disease, stable angina, FC. Atherosclerotic cardiosclerosis. Atherosclerosis of the aorta and its valves with aortic stenosis 1 st. Paroxysmal atrial flutter. Heart failure IIA stage with preserved left ventricular function, II FC.

The patient was prescribed bisoprolol 2.5 mg in the morning for a long time under the control of heart rate, cardiomagnil 75 mg in the evening for a long time, losartan was recommended not to take the morning, but shift the time of drug intake to the bedtime, in the same dose – 50 mg – under the control of blood pressure.

Three months later, the patient came to the follow-up. He noted the improvement in general condition. The frequency of chest pain decreased to 1–2 times a week, according to a home blood pressure monitoring BP stabilized at 130–140/80–85 mm Hg. Dynamics of QOL and ABPM indices is presented in Tables 1–4. There is a decrease in daily BP means and hypertension load, especially for DBP. Daily DBP and MAP profiles transformed from non-dipper to dipper; the daily profiles of SBP and PP remain non-dipper, but, in comparison with the baseline values, the degree of their night-time reduction has increased, which also can be considered as a positive dynamics. Repeated QOL survey showed a significant improvement in the mental health component.

Thus, we achieved the SBP, MAP and PP daily means reduction and target levels for DBP and normalization of DBP and MAP daily profiles only by shifting the time of antihypertensive drug – losartan – administration.

Table 1

BP means according to ABPM data

Parameter	Visit 1 (20.01.16)	Visit 2 (30.03.16)	Normal ranges
24-h period			
SBP mean, mm Hg	148	138	90–130
DBP mean, mm Hg	84	75	60–80
MAP mean, mm Hg	110	99	80–95
PP mean, mm Hg	65	63	no more then 46
Awake period			
SBP mean, mm Hg	150	140	90–135
DBP mean, mm Hg	86	77	60–85
MAP mean, mm Hg	112	101	80–95
PP mean, mm Hg	65	63	no more then 46
Asleep period			
SBP mean, mm Hg	142	129	80–120
DBP mean, mm Hg	78	66	50–70
MAP mean, mm Hg	104	90	80–95
PP mean, mm Hg	65	62	no more then 46

Table 2

Hypertension load indices according to ABPM data

Parameter	Visit 1 (20.01.16)	Visit 2 (30.03.16)	Normal ranges
24-h period			
Time index SBP. % (duration of BP excess)	91,6	67,8	up to 15
Time index DBP, % (duration of BP excess)	67,0	22,9	up to 15
Square index SBP, mm Hg/h (hyperbaric index)	438,9	213,3	up to 15
Square index DBP, mm Hg/h (hyperbaric index)	111,1	34,1	up to 15
Awake period			
Time index SBP. % (duration of BP excess)	87,2	61,6	up to 15
Time index DBP, % (duration of BP excess)	58,9	22,6	up to 15
Square index SBP, mm Hg/h (hyperbaric index)	254,1	139,6	up to 15
Square index DBP, mm Hg/h (hyperbaric index)	52,0	18,2	up to 15
Asleep period			
Time index SBP. % (duration of BP excess)	98,9	80,0	up to 15
Time index DBP, % (duration of BP excess)	80,2	23,5	up to 15
Square index SBP, mm Hg/h (hyperbaric index)	184,8	73,7	up to 15
Square index DBP, mm Hg/h (hyperbaric index)	59,1	15,9	up to 15

Table 3

Daily BP pattern according to ABPM data

Sleep-time relative BP decline	visit 1 (20.01.16)	visit 2 (30.03.16)
SPB	5,4 % non-dipper	7,8 % non-dipper
DBP	9,4 % non-dipper	13,9 % dipper
MAP	7,2 % non-dipper	10,2 % dipper
PP	0 % non-dipper	1,58 % non-dipper

Table 4

Health-related quality of life (in points by SF-36 scale)

Scale	visit 1 (20.01.16)	visit 2 (30.03.16)
Physical Functioning (PF)	80	75
Role- Physical (RP)	0	0
Bodily Pain (BP)	41	41
General Health (GH)	60	75
Physical Component Summary (PCS)	40,43	39,39
Vitality (VT)	75	75
Social Functioning (SF)	50	87,5
Role- Emotional (RE)	0	100
Mental Health (MH)	64	88
Mental Component Summary (MCS)	36,75	58,74

CONCLUSIONS

In the treatment of patients with hypertension it is important not only to achieve target BP levels, but also to restore and maintain its physiological circadian rhythm, including, as the present case reports, DBP. AH control without antihypertensive drugs dosage increase is possible only within chronotherapeutic approach.

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NOONAN'S SYNDROME

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The clinical case an adult patient with rare genetically heterogeneous disorder combine with congenital heart diseases and multiple stigmas of disembryogenesis, currently presenting mostly with signs of pulmonary hypertension have been reviewed. Patient is presented with definitive Noonan's syndrome according scoring system of Van Der Burgt (has 2 major criteria). The data of the laboratory and instrumental diagnostic methods, clinical diagnosis, selection of the optimized treatment and modification of the habit of life are given.

KEY WORDS: noonan's syndrome, Turner phenotype, unusual external features**,** pulmonary hypertension

СИНДРОМ НУНАН

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Розглянуто клінічний випадок дорослого пацієнта з рідкісним генетичним захворюванням, що поєднується з вродженими вадами серця і множинними стигмами дізембріогенезу, що на даний час переважно проявляється симптомами легеневої гіпертензії. Пацієнт представлений з визначеним діагнозом синдром Нунан згідно з системою бальної оцінки Ван Дер Бургу (має 2 головні критерії). Наведено дані лабораторних та інструментальних методів дослідження, описана діагностика, постановка клінічного діагнозу, вибір оптимальної тактики лікування та модифікація способу життя.

КЛЮЧОВІ СЛОВА: синдром Нунан, фенотип Тернера, незвичайні зовнішні ознаки, легенева гіпертензія

СИНДРОМ НУНАН

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Рассмотрен клинический случай взрослого пациента с редким генетическим заболеванием, сочетающийся с врожденными пороками сердца и множественными стигмами дизэмбриогенеза, в настоящее время преимущественно проявляющийся симптомами легочной гипертензии. Пациент представлен с определенным диагнозом синдром Нунан согласно системе балльной оценки Ван Дер Бурга (имеется 2 главных критерия). Приведены данные лабораторных и инструментальных методов исследования, описана диагностика, постановка клинического диагноза, выбор оптимальной тактики лечения и модификация образа жизни.

КЛЮЧЕВЫЕ СЛОВА: синдром Нунан, фенотип Тернера, необычные внешние признаки, легочная гипертензия

INTRODUCTION

Noonan syndrome (NS) is a pleomorphic autosomal dominant disorder with cardinal features such as short stature, distinctive facial dysmorphia, webbed neck, and heart defects. NS is a relatively common congenital disease that affects both males and female equally [1].

In 1962, a pediatric cardiologist Jacqueline Noonan presented a clinical study of associated non-cardiac malformations in children with congenital heart disease at the Midwest Society for Pediatric Research, where she also

described nine patients that shared distinctive facial features and who had a short stature, pulmonary stenosis and significant chest deformities [2].

Synonyms of NS are: female pseudo-Turner syndrome, male Turner syndrome, Turner phenotype with normal chromosomes (karyotype) [3].

It is believed that between approximately 1 in 1000 and 1 in 2500 children worldwide are born with NS [1, 4].

NS is caused by a genetic mutation and types are based on the gene in which mutation has occurred. NS divides on 5 types: NS1 – PTPN11 (50 %), NS2 – unknown (autosomal recessive), NS3 – KRAS (less than 5 %), NS4 – SOS1 (13 %), NS5 – RAF1 (3–17 %) [1].

There are 3 most common features of NS: 1) unusual facial features, 2) short stature (restricted growth), 3) heart defects present at birth (congenital heart disease). Unusual facial features include: a broad forehead, drooping eyelids (ptosis), wider-than-usual distance between the eyes, short, broad nose, low-set ears that are rotated towards the back of the head, a small jaw, a short neck with excess skin folds, lower-than-usual hairline at the back of the head and neck [3,4].

Thus, the combination of multiple unusual facial features (different stigmas of disembryogenesis) and congenital heart defects could indicate the presence of a rare genetically determined congenital disease with a high degree of probability. This article focuses on one of such cases.

CLINICAL CASE

The patient K., a man born in 1993, was admitted to the STPI «Central clinical hospital «Ukrainian railway»» cardiology department in March, 2016 with complaints of dyspnea (observed during physical exertion (climb to the 7th floor) and relieved at rest); dizziness – when he changes his body position from horizontal to vertical (orthostasis); general fatigue.

HISTORY OF DISEASE

Congenital heart disease was diagnosed in the hospital at birth. In 2002 an endovascular dilation of valvular stenosis of the pulmonary artery was made. He is being under heart surgeon supervision at the Institute of MHS Amosov with diagnosis: Condition after endovascular dilation of valvular stenosis of the pulmonary artery. Residual pulmonary stenosis, secondary atrial septal defect. Last consultation on 03.07.13 he was recommended to undergo a conductive plastic surgery by an occluder for the atrial septal defect.

ANAMNESIS VITAE

He was born in a full family. Leads a healthy lifestyle, patient does not smoke or drink, getting enough nutrition, has good living conditions. Patient denies tuberculosis, malaria, viral hepatitis, sexually transmitted diseases and AIDS: also denies allergic reactions to drugs. In 2001 he underwent tonsillectomy. Hereditary: father – essential hypertension, IHD, MI.

PHYSICAL EXAMINATION

General condition is satisfactory, consciousness is clear, emotionally stable, optimistic mood. Height = 168 cm, Weight = 70 kg. Skin is normal colored, without any scars. Peripheral lymph nodes, the thyroid gland are not palpable. Musculoskeletal system present with a lot signs of unusual features: triangular face shaped, webbed neck, small chin, thick helix, incomplete folding ears, low set and widely spaced nipples, webbed neck; also another unusual facial signs – low posterior hairline, ocular hypertelorism, drooping of the upper eyelids (ptosis), «hooded» eyelids.

Auscultation over the lungs is clear, vesicular breathing. Auscultation of the heart-continues diffuse parasternal systolic murmur, pulmonary valve diastolic murmur, tricuspid valve systolic murmur, mitral valve mild systolic murmur, aortic valve-normal sounds (no evidence of murmur). BP sin = 112/74 mmHg, BP dextr = 110/72 mm Hg. Abdomen is normally sized, soft and painless. Liver and spleen remain impalpable. Tapping symptom is negative on both sides.

REFERRAL DIAGNOSIS

Male Turner syndrome. Congenital heart defect. Pulmonary hypertension.

RESULTS OF LABORATORY AND INSTRUMENTAL DIAGNOSIS

Complete blood count (01/03/16): slight elevation in RBCs, HGB, HCT values may be due to compensatory mechanism in response to decrease in O2 saturation due to PH.

Urinalysis (01/03/16): all figures were in normal range.

Biochemical analysis (01/03/16): all figures were in normal range.

Electrocardiography (ECG) (01/03/16): showed irregular sinus rhythm with heart rate 47 bpm, sinus arrest during inhale (pause 3035 ms) – asymptomatic, RBBB morphology, right ventricular hypertrophy with strain.

Holter ECG monitoring (24 h) (03/03/16): showed sinus rhythm with RBBB average daily HR – 74 beats / min and mean nocturnal HR – 54 bpm, recorded maximum HR – 181 bpm (patient «ran up the stairs») and minimal HR – 38 bpm at 05:22:05. Circadian index 1,37 (N 1,24–1,44). During the entire period of monitoring were recorded frequent sinoatrial blockades II degree Mobitz 1 and Mobitz 2 with a maximum pause – 1832 ms at 23:19. Also a single ventricular premature beats were recorded (total 2).

Echocardiography (01/03/16): signs of pulmonary valve stenosis 1nd degree, RV hypertrophy, dilation of the RV and RA. Mitral regurgitation 1st degree, tricuspid and pulmonary valve regurgitation 1st and 2nd degree, pulmonary hypertension 1st stage. Defect of the central part (8.3 mm) of atrial septum with left to right shunt. Additional chord in the left ventricular lumen, not hemodynamically significant.

Ultrasonography of the abdomen (01/03/16): kidney salt diathesis, right nephroptosis; other parameters were in the normal range.

Consultation of heart surgeon-arrhythmologist (10/09/16): according to Holter ECG with solitary episodes of SA blockades and solitary asymptomatic episode of sinus arrest (01.03.16) are not clinically significant. There are no indications for pacemaker implantation.

RECOMMENDATIONS FOR FURTHER EXAMINATION

Genetic counselling (determines the type gene in which mutation has occurred and karyotype)

Fertility issues **(**General physical examination and medical history, Semen analysis, Hormone testing ets.).

Neuropsychological and behavioral issues (intelligence tests, personality tests, perceptual-motor/memory tests).

Coagulation screening (a prothrombin time, and an activated partial thromboplastin time).

Thyroid screening (TSH, T3, T4).

Dental screening to determine the presence of other abnormalities.

Vision screening (external inspection of the eye and lids, ocular motility assessment, pupil examination, red reflex examination, visual acuity testing, ophthalmoscopy) [1–4].

CLINICAL SYNDROMES

1. Congenital heart defects
2. Pulmonary hypertension
3. Erythrocytosis, hemoconcentration
4. Arrhythmias (persistent SA blockade)
5. Heart failure
6. Multiple stigmas of disembryogenesis

CLINICAL DIAGNOSIS

Main:

Noonan's syndrome (triangular face shaped, webbed neck, thick helix, widely spaced nipples, low posterior hair line, ocular hypertelorism, ptosis, erythrocytosis).

(CHD: condition after endovascular dilatation pulmonary valve stenosis (2002).

Residual pulmonary valve stenosis I degree (mild severity).

Pulmonary valve insufficiency II degree (moderate severity).

Secondary atrial septal defect with left to right shunt.

Transient sinoatrial block II degree type I.

Complication:

Pulmonary hypertension I class.

Right heart failure I FC, stage B.

CASE MANAGEMENT

- Meldonium – 5,0 IV.
- Trimetazidine – 35 mg twice a day.

RECOMMENDATIONS FOR LIFESTYLE MODIFICATION

1. Reduce salt intake.
2. Reduce intake of sugar-sweetened beverages and foods.
3. Eat vegetables and fruits and limit juice intake.
4. Patient requires sensible advice about general activities of daily living and need to adapt to the uncertainty associated with a serious chronic life-threatening disease.
5. Immunization of PAH patients against influenza and pneumococcal infection is recommended.
6. Supervised exercise training should be considered in physically deconditioned PAH patients under medical therapy.

7. In elective surgery, epidural rather than general anesthesia should be preferred whenever possible.

8. Excessive physical activity that leads to distressing symptoms is not recommended in PAH patients [1–4, 5].

RECOMMENDED TREATMENT ACCORDING LAST GUIDELINES

- Sildenafil 25 mg in the morning for treatment pulmonary hypertension and preventing progression of it [5].
- Perindopril 1–2 mg in the evening to prevent myocardial remodeling [6].
- Regular cardiac screening [2].
- Planned conductive plastic surgery by an occluder for the atrial septal defect to prevent RV failure and as a result fluid retention.

PROGNOSIS

Noonan's syndrome is a genetic disorder and prognosis for recover is an unfavorable. According to the medical literature, physicians who specialize in diagnosing and treating heart abnormalities (cardiologists) should suspect the possibility of NS in any individuals who have congenital pulmonary valve stenosis, unusual facial features and certain eye abnormalities typically found even in the more mild cases (e. g., ptosis, epicanthic folds, ocular hypertelorism) [4].

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Review

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ARTERIAL HYPERTENSION AND MEDICAL SUPPORT OF PATIENTS WITH PERMANENT PACEMAKERS

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The review is devoted to clinical problems of arterial hypertension (AH) in patients with implanted pacemakers (EKS) and cardiac resynchronization therapy (CRT). Indications for pacemaker implantation and CRT are considered, especially the purpose and effectiveness of angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor antagonists (ARA, sartans), beta-blockers (BAB), diuretics, calcium channel blockers. We prove that the CRT and cardiac pacing and do not cancel, bur modify drug therapy of AH.

KEY WORDS: cardiac pacing, arterial hypertension, therapy of AH

АРТЕРІАЛЬНА ГІПЕРТЕНЗІЯ ТА МЕДИКАМЕНТОЗНА ПІДТРИМКА ПАЦІЄНТІВ З ІМПЛАНТОВАННИМИ ЕЛЕКТРОКАРДІОСТИМУЛЯТОРАМИ

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Огляд присвячений клінічним проблемам артеріальної гіпертензії (АГ) у пацієнтів з електрокардіостимуляторами (ЕКС) та кардіоресенхронізуючою терапією (КРТ). Розглянуто показання до імплантації ЕКС і КРТ, особливості призначення та ефективність діуретиків, бета-блокаторів, антагоністів кальцію, інгібіторів ангіотензіперетворюючого ферменту, антагоністів рецепторів ангіотензину II. Доведено, що ЕКС і КРТ не скасовують, а модифікують медикаментозну терапію АГ.

КЛЮЧОВІ СЛОВА: електрокардіостимулятори, артеріальна гіпертензія, терапія АГ

АРТЕРИАЛЬНАЯ ГИПЕРТЕНЗИЯ И МЕДИКАМЕНТОЗНОЕ СОПРОВОЖДЕНИЕ ПАЦИЕНТОВ С ИМПЛАНТИРУЕМЫМИ ЭЛЕКТРОКАРДИОСТИМУЛЯТОРАМИ

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Обзор посвящен клиническим проблемам артериальной гипертензии (АГ) у пациентов с имплантированными электрокардиостимуляторами (ЭКС) и кардиоресенхронизирующей терапии (КРТ). Рассмотрены показания к имплантации ЭКС и КРТ, особенности назначения и эффективность диуретиков, бета-блокаторов, антагонистов кальция, ингибиторов ангиотензипревращающего фермента, антагонистов рецепторов ангиотензина II. Доказывается, что ЭКС и КРТ не отменяют, а модифицируют медикаментозную терапию АГ.

КЛЮЧЕВЫЕ СЛОВА: артериальная гипертензия, электрокардиостимуляторы, терапия АГ

INTRODUCTION

Nowadays, permanent endocardial pacing (pacing) and cardiac resynchronization therapy is the most recognized and effective method of treatment for severe arrhythmias and conduction disorders, as well as for the resistant chronic heart failure (CHF). Pacing significantly improves the quality of patient's life and reduces mortality.

The world's first pacemaker implantation was performed by A. Senning at the Karolinska Hospital in 1958, which was the impetus for the development and the elaboration of new highly

effective method of treatment for bradyarrhythmias [1–2].

In international practice, 5-letter code is used to describe the program of a pacemaker, which is a joint development of the working groups of the North American Society of Pacing and Electrophysiology (NASPE) and the British group of Pacing and Electrophysiology (BPEG), known as the common code NBG-NASPE/BPEG.

The first letter denotes a stimulated heart chamber (A-atrium-, V-ventricle, D-two chambers, O-absence of stimulation of the heart function).

The 2nd letter indicates detectable heart chamber (A-atrium, V-ventricle, D-two chambers, O-absence of stimulation of the heart function).

The 3rd letter indicates the method of response (I-inhibitory, T-trigger, D-double, O-absence).

The 4th letter indicates the device programmability features and the availability of frequency adaptation (R-simple, M-multiprogrammability, C two-way communication, R-frequency adaptation, O-absence).

The 5th letter defines antiarrhythmic function (P-antiarrhythmic stimulation, S-defibrillation, D-double, O-absence) [3–4].

The main indications for pacemaker implantation are atrioventricular (AV) block, sick sinus syndrome (SSS), bifascicular and three fascicular blocks, myocardial infarction (MI) and its associated arrhythmias, paroxysmal symptomatic ventricular and supraventricular tachycardia, and high functional classes (FC) of chronic heart failure (CHF) and hypertrophic cardio-myopathy (HCM) [5–6].

The main purpose of pacing is the simultaneous activation of both ventricles, in order to improve the mechanical efficiency of the ventricles [7–8]. Pacemaker implantation significantly increases the left ventricular ejection fraction and reduces the frequency of hospitalization [9–11].

Arterial hypertension (HT) is the leading problem of modern cardiology, due to its prevalence and adverse complications [12–13].

AH is the most common comorbidity in patients with a pacemaker, which has a signi-ficant impact on its current, and be for all on, the control of blood pressure (BP) [14].

AH is diagnosed at the level of systolic blood pressure (SBP) > 140 mm Hg = and / or diastolic blood pressure (DBP) ≥ 90 mm Hg. If an increase is stable and confirmed by regular measurements of BP (not less than 2–3 times on different days for 4 weeks) [15], as evidenced by data from randomized controlled trials (RCTs) on the therapeutic benefits of lowering BP, since these indicators [16].

The prevalence of AH in the range 30–45 % of the general population, with a sharp increase in the aging, without any systemic trends to changes in BP in the last ten years [17–20]. According to the official statistics, more than 11 million people were registered in 2007 in Ukraine, which amounts for 29.9 % of the adult population [15].

According to the latest recommendations of the European Association of Hypertension and the European Cardiology Association (2013), they distinguish 3 grades of AH according to the level of blood pressure:

- Grade 1 (mild) – 140–159 mm Hg SBP, DBP 90–99 mm Hg.
- Grade 2 (moderate) – SBP 160–179 mm Hg, DBP 100–109 mm Hg.
- Grade 3 (severe) – SBP ≥ 180 mm Hg, DBP> = 110 mm Hg.
- Isolated AH – SBP ≥ 140 mm Hg, DBP < 90 mm Hg.

The classification of organ damage is used to establish the stage of AH. This classification was developed by WHO experts (1963–1993) and adopted in Ukraine in 1992, according to the order of Ministry of Health of Ukraine № 206 from 30.12.1992. It is recommended for use according to the order № 247 from 1.08.1998 [15].

I stage – there is no objective evidence of target organ damage.

Stage II – there is objective evidence of target organ damage, with the absence of symptoms:

- Left ventricular hypertrophy (LVH)
- Generalized narrowing of the retinal arteries
- Microalbuminuria
- Atherosclerotic vascular disease

Stage III – there is objective evidence of target organ damage, the presence of symptoms on their part or dysfunction:

- Heart – heart attack (myocardial infarction), heart failure IIA-III st.
- Brain – a stroke, transient ischemic attack, vascular dementia, acute hypertensive encephalopathy.

- Fundus – hemorrhage and exudates in the retina and swelling of the optic nerve.
- Kidneys – proteinuria and / or the concentration of creatinine in the blood plasma > 133 mmol/L in males and > 124 mmol/l in women.
- Vessels – aortic dissection, occlusive peripheral arterial disease.

Stroke is the main cause of death in patients with AH [21]. Approximately two-thirds of strokes and half of all cases of IHD are due to AH, it becomes the cause of 7 million deaths and 64 million cases of disability per year [22–23].

In general the implantation of the pacemaker has a positive effect on patients' quality of life [24–27]. However, due to the improvement of the pumping function of the left ventricle, can cause instability of BP [28], as a result the progression of AH [29–31]. In this regard, drug therapy is not canceled, but should be modified. Drug therapy of AH in patients with implanted pacemaker and CRT is still poorly investigated.

ATRIOVENTRICULAR BLOCK

Atrioventricular block (AV block) is characterized by a delay or discontinuation of impulses through the AV node, as a result of the compensatory response in the form of the progression of AH, that was partially confirmed in studies [32–33]. According to [34], AH is the most common risk factor in patients with AV block.

There are three degrees of AV block. AV block of the 1st degree is abnormal prolongation of the interval P-R more than 0.2 sec., the second degree is divided into 2 types. The I type is characterized by progressive elongation of the P-R interval to the blocked contraction and is associated with a narrow QRS complex, II type – fixed Interval P-R before and after the blocked complexes and associated with a wide QRS complex. In a far-reached AV block of the 2nd degree, two or more successive P waves are not conducted. In the 3rd degree AV conduction is absent [35–36].

In patients with hypertension occurs the development of CHF and increases the risk of sudden cardiac death due to prolonged asystole and bradycardia [37–38].

Cardiac pacing is the only accepted method of treatment of AV block high degrees [39].The DDD mode is the choice of pacing mode for patients with stored chronotropic sinus node function [40].

Cardiac pacing in patients with AV block, significantly improves the quality of their life and increases their physical performance [41], nevertheless, due to the normalization of the pump function, may cause progression of AH. These data partially was confirmed in the study [34], in which was found that 29.6 % of patients with normal BP before cardiac pacing had AH after the implantation, mostly first degree. In 48.1 % of patients with AV block with high BP before cardiac pacing, in the postoperative period occurred AH of the second degree.

SICK SINUS SYNDROME

Sick sinus syndrome(SSS), also called Sinus node dysfunction, is a group of abnormal heart rhythms (arrhythmias) presumably caused by a malfunction of the sinus node which is clinically manifested in the form of significant bradycardia inadequate growth of the heart rate, progression of AH, poor exercise tolerance, dizziness, fatigue [42]. In some cases, there is a tendency to supraventricular tachyar-rhythmia (brady-tachy – form of SSS) [43–45]. The incidence of SSS increases due to the aging of the population [46].

Cardiac pacing is the leading choice of treatment for the patients with SSS and it significantly reduces the symptoms, but without changes in survival [47].

In patients with SSS preferably one- or two-chamber atrial pacing, particularly in patients with atrial fibrillation (AF) and the influence on patients' quality of life [44, 48].

Stimulation in the AAIR mode is associated with a higher incidence of paroxysmal atrial fibrillation, so DDDR mode is more appropriate in such patients [49]. The Albertsen and Nielsen’s resource [50] demonstrated that the AAIR mode exceeds DDDR and reduces episodes of AF. According to DANPACE resource, DDDR mode is more effective for treatment patients with SSS and comorbid disorders [51]. Dual-chamber pacing increases life expectancy and improves its quality [52–53].

Cardiac pacing in patients with AH and SSS leads to stabilization of heart rate and intracardiac hemodynamics [54], however there is destabilization of BP and progression of AH on this background. Only in the one study these data were confirmed [55], in which was found

out increase of SBP in patients with SSS after the cardiac pacing.

INTRAVENTRICULAR BLOCKS

Intraventricular blocks (IVB) occurred in the violation of intraventricular conduction, partly or complete block of one, two and three branches of the bundle of His. There are also various combinations of full and partial blocks of branches of the bundle of His.

IVB occur as a result of anatomic abnormalities (malformation, inflammation, sclerosis, degeneration) or the development of a functional block (for supraventricular tachyarrhythmia and others), always complicated by CHF and prone to progression [56]. A part of patients can have an increase of SBP and progression of hypertension [57–58]. Especially unfavorable prognosis has combination the block of the right and anterior branch of the left bundle of His.

Often is noted syncope in patients with block of two branches of the bundle of His.Despite the fact that syncope may be repeated, it is not associated with an increased risk of sudden death. Pacing in such patients exempt from transient neurological symptoms, but did not reduce the incidence of sudden death [59].

Biventricular stimulation in patients with IVB provides a coordinated contraction of ventricles, it reduces the width of the QRS complex, and reduces the intraventricular and interventricular asynchrony [60].

There is an increase of SBP in patients with the block of two branches of the bundle of His, which was demonstrated in the research [61], these data indirectly indicates the progression of AH.

PAROXYSMAL VENTRICULAR AND SUPRAVENTRICULAR TACHYCARDIAS

Paroxysmal ventricular and supraventricular tachycardia – type of arrhythmia are characterized by palpitations (paroxysms), with a heart rate from 140 to 220 or more per minute, arising under the influence of ectopic pulses, which leads to the replacement of normal sinus rhythm. As a rule, they are accompanied by increase of BP and progression of AH. Ectopic impulses can be generated in the atrium, AV node or ventricles [62–63].

Cardiac pacing may be useful for the treatment of patients with recurrent symptomatic ventricular and supraventricular tachycardia [59, 64]. Antiarrhythmic device can detect tachycardia and automatically activate the stimulation, or respond to an external trigger. In some patients with long QT syndrome recurrent, brady-form of VT can be prevented by the overdrive stimulation. It is described that the combination of atrial pacing and beta-blockers shortens the QT-interval and helps to prevent sudden death [65].

Besides that ectopic ventricular activity may also be inhibited by such stimulation, severe and symptomatic arrhythmia is rarely preventable [66].

In a multicenter, randomized clinical trial SAFARI was demonstrated the safety and efficiency of preventive pacing algorithms that was designed for the prevention of AF in patients with bradycardia and paroxysmal AF. The biggest efficiency was achieved with initial frequent paroxysms of AF [67].

Bifocal stimulation of the right atrium or alternative monofocal stimulation of non-traditional outlets (eg. interatrial septum or the Bachman bundle), may provide additional advantages compared with a monofocal stimulation of the right atrial appendage in patients with symptomatic drug-refractory atrial fibrillation and concomitant bradyarrhythmia. In patients with SSS and intraatrial block (P is greater than 160 ms) biatrial stimulation can reduce the incidence of recurrent AF [68].

The research [69] described an increase of SBP and a slight increase of DBP in patients with AF after the cardiac pacing, which indirectly indicate the progression of AH.

HYPERTROPHIC CARDIOMYOPATHY

Hypertrophic cardiomyopathy (HCM) is a genetic cardiovascular disease. It is defined by an increase in left ventricular wall thickness that is not solely explained by abnormal loading conditions. It is usually accompanied by AH high degrees. This is the most common of genetically caused cardiomyopathy (20 per 10 000) [70].

According to the results of the echocardiographic screening of the population in Ukraine (15 700 people), that was made by A.I. Minakov, occurrence of HCM was 0,47 %, that was much more than in other countries.

Invasive methods of treatment include implantation of a defibrillator for patients with a high risk of sudden death and two-chamber AV-stimulation.

In the early nonrandomized studies was demonstrated the reduction of the gradient between the left ventricle and outflow tract, in patients with dual-chamber pacing with a short AV delay, and a reduction of symptoms in some patients with hypertrophic obstructive cardiomyopathy [59, 71].

The research, including 8 people with dual-chamber pacing for a long period of time, found out the reduction of the gradient even after the cessation of the stimulation. That helped suggest that due to the stimulation happened ventricular remodeling. Two randomized studies have shown the improvement in subjective quality of life approximately in 50 % of the patients, which, however, was not associated with a decrease of the gradient and placebo effect. A third randomized study did not show any improvement in the quality of life in patients with a pacemaker, although it has been suggested that stimulation in elderly patients (over 65 years) was more effective [59, 71–72]. A small group of patients with obstructive HCM was held the VDD-stimulation with premature ventricular excitation, i. e. the short AV delay. In this group was observed an increase in exercise tolerance, cardiac reserve and improvement of clinical symptoms. In some patients was reduced efficacy of pacing at a high rate of atrial rhythm, fast AV-holding and congenital anomalies of the mitral valve.

Nowadays there is practically no evidence that pacing stops further progression of the disease and improves survival or quality of life [73].The efficiency of pacing is determined mainly by the severity of the gradient (more than 30 mm Hg at rest and more than 50 mm Hg under a load). [59]

Cardiac pacing reduces the adverse hemodynamic disturbances, which are caused by obstruction the outflow tract of the left ventricular. In the research [74–75] was described the increase of the diameter and the volume of the outflow tract of the left ventricle, as a result of the generation of the excitation of the LV, in the course of this was observed the reduction of SBP and the increase of DBP, which indirectly indicates the progression of AH.

CHRONIC HEART FAILURE

Chronic heart failure (CHF) is one of the most severe and prognostically unfavorable complications of diseases of the cardiovascular system. One of the main components of the formation of CHF is the remodeling of the heart, including the processes of hypertrophy and dilatation of the myocardium, leading to changes of systolic and diastolic function of the LV, as a result of the progression of AH. In most patients, medical therapy is ineffective [76].

The main causes of death in patients with CHF are the violation of the pumping function of the heart and SCD. According to the ATLAS data which was made in Great Britain, the cause of 33–50 % of all deaths is HF.

Modern devices of recent generations for treatment CHF include ACD with cardiac resynchronization therapy (CRT) which leads to protect the patient at high risk for life-threatening arrhythmias, improve the quality of life and clinical outcomes in HF. The common goal of such combined devices is to slow the progression of HF, reduce the time of treatment in hospital and the prevention of SCD [60].

Indications for cardiac pacing and CRT in patients with heart failure are patients with CHF III-IV functional class according to the NYHA classification, the ejection fraction of the left ventricular (LVEF) less than or equal to 35 %, despite the optimal medical therapy, in the presence of sinus rhythm and the duration of QRS more than 120 ms, [77] the duration of QRS more than 120 ms and of the left bundle branch block (LBBB), or the duration of QRS more than 150 ms, independently of the morphology of QRS [78–79].

Patients with less severe HF (ischemic cardiomyopathy FC I or II non-ischemic cardiomyopathy FC II), EF < or = 30 % and QRS > or = 130 ms have also benefit from pacing [80]. Reduced the systolic function of the right ventricular before implantation – one of the most important performance criteria of pacing [81].

Cardiac pacing, and to a much greater extent displacing its CPT, in patients with CHF and dyssynchrony improves such hemodynamic parameters as the left ventricular fraction (LVEF), the end-diastolic and the end-systolic volume and of left ventricular, the stroke volume of the left ventricle, pulmonary artery pressure and the 6-minute test walk away. [82–85].

In studies [86–87], the transition from the right ventricular pacing to biventricular significantly improved echocardiographic parameters such as the function of the left

ventricular [88–89], reduction of dyssynchrony and reduction of symptoms typical for CHF [90], regardless of ischemic or nonischemic etiology of CHF. Sideris S. et al. proved the effectiveness of CPT in the transition from right ventricular stimulation in the form of reduction of CHF FC, LVEF increased, reduction of the QRS complex, and improved the data of 6-minute walk test [91].

It should be noted that among the majority of patients suffering from CHF, only 1/3 of the patients received only slight improvement [92–93]. In the research [94] was noticed that 81 % of patients on the background of cardiac pacing had an increase of SBP, which indirectly indicates the progression of hypertension.

MEDICATION SUPPORT OF PATIENTS WITH CARDIAC PACING AND AH

The importance of a patient's management after the implantation of antiarrhythmic device cannot be overestimated. A modern pacemaker is a multiple programmable device with a large number of therapeutic and diagnostic functions, so it needs regular inspection and adjustment [95–96]. When it comes to the monitoring of patients with an implanted pacemaker, it should be an implied assessment of the entire pacing system, not just a single device. As the stimulation system consists of 3 main units: the pacemaker, the electrodes and the patient's heart, the assessment should be carried out of all of these units [97]. The main problems when checking the system of stimulation in general are analysis of the functioning of the pacemaker and the electrode(s) and timely detection and elimination of violations in the stimulation system; assessing the adequacy of installed programs of stimulation and the correction of parameters; the assessment of the state of the power supply; timely detection and elimination of complications; education [98].The frequency and method of observation depends on many factors, including different cardiovascular diseases and medical problems, period of a pacemaker implantation. The first check is carried out in 1.5–3 months after surgery, in terms of formation of the chronic stimulation threshold, when it becomes possible to control the final energy stimulation parameters. It is generally accepted HCFA guidance (1984), according to which patients with a single-chamber pacemaker after implantation an appointment is recommended to be twice within six months, then annually, with two-chamber pacemaker – twice for 6 months, then every six months. Regular dynamic monitoring of patients with a pacemaker and CRT is a mandatory procedure, which provides timely detection, diagnosis and correction of irregularities in their work with the optimization of pacing program, to achieve the best clinical effect and to prolong the lifetime of the device [98].

Cardiac pacing significantly extends the capabilities of drug therapy, but at the same time there are additional requirements for ambulatory monitoring of patients after implantation [99–100].

Drug support of patients with cardiac pacing, as a rule, generally meets with the standards [101]. However, we must consider the impact of drugs on the threshold of pacing, the result of which can become serious hemodynamic disturbances, pacing threshold increase of potassium, b-blockers, calcium channel blockers, quinidine, aymalin, izuprel, izadrin, and lower – prednisolone, norepine-phrine, ephedrine [102].

It should be noted that the data on the effect of many drugs (calcium channel blockers, ACE inhibitors, angiotensin II receptor antagonists, and others.) used for the treatment of patients with cardiovascular disease and an implanted pacemaker, today is not enough. In the medical support of patients with hypertension and an implanted pacemaker is used angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor antagonists (ARA, sartans), beta-blockers (BAB), diuretics, calcium channel blockers. For the treatment of comorbid cardiovascular diseases is used ivabradine, digoxin, statins, warfarin, dabigatran, rivaroxaban, apixaban, aspirin, amiodarone, which may influence the course of hypertension [103–104].

Systematic observation of patients with pacemaker and CRT, and the effectiveness of therapy depending on the QRS complexes and QTc were first described in the works [105–106]. According to the date [106] after the pacemaker implantation the QRS duration did not change – in 33 %, shortening – in 22 %, elongation – in 45 % of cases, at CRT extension occurred in 90 % of cases, while with the increase of the class of QRS duration increased the frequency of appointments of ACE inhibitors, BAB, diuretics. According to the date [105] after pacemaker implantation in 55 of cases occurred the elongation of the QTc

complex that was associated with higher degrees of hypertension. However, the therapeutic support of patients with AH and implanted pacemaker and CRT is still poorly investigated.

DIURETICS

Thiazide diuretics, appointed in small doses, not only as effective as the other groups of antihypertensive drugs, but also prevent the development of cardiovascular complications in patients with AH [66].

In the TOMHS and VACS researches was shown that hydrochlorothiazide, chlorthalidone, indapamide induced a good anti-hypertensive effect. In the long-term therapy drugs were effective in 50–70 % of patients with AH [108]. However, in the research [109] was shown that hydrochlorothiazide reduced SBP only at 7.5 mm Hg and DBP – 4.6 mm Hg.

In the LIVE study was shown, that therapy with indapamide resulted in a significant decrease in LVM, there was no similar results in the group of enalapril. Indapamide also largely reduced the severity of the left ventricular hypertrophy than enalapril [110].

The use of loop diuretics for AH is largely limited for the treatment of hypertensive crises, and concomitant severe cardiac and kidney failure. Potassium-sparing diuretics, in most cases do not have an independent value in the treatment of hypertension and is used in combination with thiazide or loop diuretics [15, 111].

Researches on the appointment of diuretics in patients with AH and a pacemaker were not carried out practically. According to researches [105, 107] the frequency of the use of diuretics increased in the acute postoperative period after cardiac pacing. The study, [112] showed that the use of furosemide in patients with pacemaker significantly reduced BP.

BETA-BLOCKERS (BAB)

Recently, BAB was the drugs of first-line treatment of AH [113]. However, in the studies [114, 115], was noted that the BAB conceded to calcium antagonists in terms of overall mortality and cardiovascular events. However, in a large meta-analysis made by Law et al, was shown, that the start of therapy with BAB as effective as the other major classes of antihypertensive agents, prevented coronary outcomes and highly effectively prevented cardiovascular events in patients with recent myocardial infarction and in patients with HF [116]. The researches [117–119] showed that BAB effectively provided cardiovascular protection.

Less efficiency BAB provided in the case of prevention from stroke [120], due to their lesser ability to reduce SBP and pulse pressure [121]. Less preventive efficacy against stroke also has ACE inhibitors [120] although the latter, according to the date [121] lower central blood pressure better than the BAB.

Carvedilol has antioxidant and anti-proliferative properties [21–22, 122], that is important to consider in terms of effects to the risk factors for cardiovascular disease and protect the target organs in patients with AH.

The most promising in the treatment of patients with AH from all members of the class of BAB is carvedilol [122]. According to the date [123], BP decreased after a single dose of carvedilol, however, the maximum antihypertensive effect developed in 1–2 weeks.

Contraindications for the appointment of BAB are asthma, clinically symptomatic bronchial obstruction, heart rate < 55–60 beats / min, sick sinus syndrome, AV-block II and III (without pacemaker implantation), SBP < 90 mm Hg.

The treatment should be started with a minimum dose that in the future increase progressively, in the case of stable hemodynamic condition of the patient, every 2–4 weeks, to the target or the maximum tolerated dose, which should be considered as optimal [3].

Indications for the BAB in patients with coronary artery disease and pacemaker besides AH, chronic heart failure, permanent AF [124, 125], is the need to suppress the ECS-induced arrhythmias. Atrial pacing electrode passes to the ventricle stimulus from the atrium and if the pacemaker has the higher limit of rate, the re-entry wave through the AV node is capable to induct the following contraction [126]. BAB has a clear beneficial antiarrhythmic effect without increasing the pro-arrhythmogenic effect in these patients [127, 128]. In patients without induced ECG and CRT arrhythmia BAB are prescribed in small doses [129].

In the MADIT-CRT study carvedilol has shown a higher efficacy against metoprolol in reduction the frequency of hospitalizations from HF and mortality. Ventricular fibrillation occurred in 22 % of patients, taking carvedilol,

compared to 26 % treated with metoprolol [128].

The research [130] showed that BAB reduced the severity of cardiac dyssynchrony in patients with HF with a normal duration of the QRS complex, especially carvedilol.

In the research [131] were given the data on the effectiveness of different doses of BAB in patients with CRT. Patients were divided into 4 groups: without BAB, taking 50 % of the target dose, and target dose. Before CRT distribution of patients was as following: without BAB – 36 %, < 50 % of the target dose – 37 %, > 50 – 20% and with a target dose – only 7 % of patients. After 6 months of CRT the ratio were – 17 %, 22 %, 28 % and 33 %, respectively. It has shown that CRT has improved the dose of BAB to achieve the optimal pharmacological effect in patients with CHF [131].

According to the data [105,107], after cardiac pacing and CRT had increased the frequency and the dose of BAB. The proper selection of a dose of BAB is a leading factor in the favorable prognosis of patients with pacemaker and AH.

CALCIUM CHANNEL BLOCKERS

Among antihypertensive drugs for first-line treatment of AH calcium channel blockers occupy a special place due to their high clinical efficiency, low frequency of side effects and good tolerance [6, 15].

According to a meta-analysis of 9 randomized controlled trials, calcium channel blockers are not inferior to traditional classes of antihypertensive drugs (diuretics, blockers, ACE inhibitors) in reduction in overall mortality, the mortality from cardiovascular causes and frequency of MI [132–134].

According to [105, 107] cardiac pacing had no effect on the frequency and dosage of the prescription of calcium channel blockers. However, there are no data on the effect of calcium channel blockers in patients with AH and pacemaker.

DIHYDROPYRIDINE DERIVATIVES (AMLODIPINE)

Reliable prevention of hypertensive crises is one of the main advantages of amlodipine. The drug allows the daily monitoring of blood pressure with a single dose [135].

Comparing the effect of amlodipine with the influence of the other calcium antagonists it shows great efficiency in BP comparing with verapamil and diltiazem. According to [136], receiving amlodipine (10.5 mg), and diltiazem (180–360 mg). The average daily BP decreased, using amlodipine to 137/84 mm Hg and diltiazem to 143/86 mm Hg.

According to the multinational study VALUE, in the group of amlodipine risk of MI was 19 % lower, also it was showed a significant reduction in the number of strokes, control of BP with monotherapy was achieved in 63 % of patients [137].

According to the date [138] amlodipine most effectively reduced the risk of total mortality, the incidence of ischemic heart disease and its complications, stroke, and it was comparable to the effectiveness with ACE inhibitors.

The research [139] showed after taking amlodipine there was an increase in heart rate in patients with cardiac pacing, for at least 15 minutes, with a decrease in systemic vascular resistance, and a statistically significant reduction in BP.

FENILALKILAMINA DERIVATIVES (VERAPAMIL)

According to the date [140], verapamil at a daily dose of 240–480 mg provided significant reduction of BP, at about 80–85 % of the patients suffering from mild (85–90 %) or moderate (75–80 %) AH. The main disadvantage of verapamil was the short duration of action. However, the introduction of a long-active form of the drug (verapamil SR) has become the solution of these problems. It also allowed taking it once a day without reducing the effectiveness of antihypertensive therapy [16].

In the research, [141] was shown that monotherapy with verapamil SR 240 mg allowed to normalize the level of diastolic BP (below 90 mm Hg) in 90 % of patients with mild AH, 77 % – with moderate hypertension and in 61 % of patients with severe AH.

Verapamil has antiarrhythmic properties and is widely used for the treatment of supraventricular arrhythmias [142].The treatment of patients, based on the use of verapamil, also effectively reduces the mortality risk of developing cardiovascular disease and stroke, as well as in the treatment of BAB [141].

Verapamil should not be prescribed in SSS, AV block, sinus bradycardia (heart rate at rest in less than 55 minutes), it is undesirable to prescribe in severe heart failure [15].

There are few studies on the effect of verapamil in patients with cardiac pacing. According to the research [143], in patients receiving verapamil at a dose of 240 mg / day in patients with AF and cardiac pacing in the DDDR mode, there was a trend of increasing in percentage of stimulation and heart rate was not reduced. There are no data on the effect of verapamil in patients with AH and cardiac pacing.

BENZODIAZEPINES DERIVATIVES (DILTIAZEM)

Benzodiazepines derivatives are good in treatment of ischemic heart disease and AH. This was confirmed by the works [144–147], which proved the ability of the drug favorably influence on the prognosis of IHD by reducing the likelihood of re-infarction, as well as the results of studies of patients with AH, in which was proved the safety of prolonged use of diltiazem and reduction of cases of stroke [145–146].

It should be noted that in the European Guidelines for the treatment of AH (2013) it was pointed out, that in patients with AH in conjunction with angina, with carotid atherosclerosis or supraventricular tachyar-rhythmia, diltiazem and verapamil – are the drugs of choice [16].

In the research [148] was noticed, that that after a single dose of diltiazem there was a significant decrease in heart rate by 7.5 %, SBP and DBP by 9.2 % and 10.9 %, respectively. After 12 weeks of monotherapy with diltiazem SBP normalized during the waking period was achieved in 61 %, in the period of sleep – 50 %, per day – at 55.5 %. DBP normalization was achieved in 66 % of patients in all presented periods.

According to the NORDIL study a significant decrease in SBP and DBP was found in the appointment of diltiazem. It confirmed the efficacy of diltiazem in the prevention of stroke, myocardial infarction, death from cardiovascular causes, which is not inferior BAB [149].

There are no studies on the effect of diltiazem in patients with a pacemaker and AH. Diltiazem in patients with pacemaker is rarely used, limited to cases without concomitant heart failure. So in the study [150], was shown that the use of diltiazem did not cause T-wave inversion.

ANGIOTENSIN CONVERTING ENZYME (ACE) INHIBITORS

ACE inhibitors are the most attractive for the treatment of AH, as they have not only the blood pressure-lowering effect, but also provide a protective effect on the target organs [151–152], which is especially important in patients with a pacemaker This class of drugs combines the advantages of high antihypertensive efficacy and good tolerability, ensuring a high quality of life with a proven cardio, vascular- and renoprotective effect and the reduction in the incidence of cardiovascular complications and increases life expectancy of patients with their long-term use [151,153].

Several studies have demonstrated the ability of ACE inhibitors to reduce LVH [154]. G.Jennings and J.Wong also noted the greatest regression of LVH in patients treated with ACE inhibitors based on 32 studies. Numerous randomized studies CONSENSUS and SOLVD have shown, that treatment with ACE inhibitors led to reduction in mortality (relative risk reduction (RR) of 27 % in CONSENSUS and 16 % in SOLVD).

The results of the PRESERVE study showed that in patients with AH and LVH receiving enalapril 20 mg 1 time per day provided not only the control of blood pressure, but also was accompanied by a remodeling of the left ventricle. Using enalapril during 1 year in 56 % of cases resulted in a normalization of myocardial mass index (IMM) LV [155–156]. Enalapril prevented dilatation and dysfunction of LV [157–159], reduced the frequency of hos-pitalizations and deaths from cardiovascular causes [160].

In the studies [161–162] was demonstrated, that the use of captopril prevented the myocardial and vascular remodeling in patients with AH and myocardial infarction.

In the PROGRESS study involving 1923 patients was registered, that perindopril significantly (by 28 %) reduced the risk of a recurrent stroke in patients with cerebrovascular diseases on the background of AH, and without it. In this study, a therapy based on perindopril not only reduced the risk of recurrent stroke, but also significantly reduced the risk of cardiovascular disease (26 %) and the risk of myocardial infarction (38 %) [163].

It was noted that perindopril had a positive impact on hemodynamic parameters in a

reduction of pressure in the right atrium and increased cardiac output [164].

In the treatment with ramipril compared with placebo, in the HOPE study, was shown an increase in the frequency of regression of LV hypertrophy and reduction of frequency of its development or progression [165].

However, ACE inhibitors can cause renal failure, hyperkalemia, symptomatic hypertension, cough, and, rarely, angioedema. Also, ACE inhibitors should be used only in patients with normal renal function and with normal levels of potassium in the blood serum [166–167].

In individual cases, there are publications on the effect of ACE inhibitors in patients with pacemaker and CRT. According to the date [107], with the increase in frequency of using ACE inhibitors was observed the lengthening of the QTc interval by 31 % in patients with cardiac pacing. According to the date [106] has increased the frequency of using ACE inhibitors in patients with cardiac pacing. The use of ACE inhibitors in patients with a pacemaker and CRT has caused an increase of LVEF and the decrease of CSR LV [168]. However, there are no data on the effect of ACE inhibitors in patients with AH and pacemaker.

ANGIOTENSIN II RECEPTOR ANTAGONISTS (ARA)

The drug of choice for the treatment of hypertension are ACE inhibitors, but the presence of side effects like a cough and angioneurotic edema, ARA recommended as alternatives in such patients [169]. ARA reduces systolic and diastolic BP by 50–70 % within 24 hours (the next day after taking the drug, the level of BP is reduced on 60–75 % of the maximum effect) [170–172].

Along with the hypotensive effect, important is the ability ARA to effect on the risk of cardiovascular complications compared with other classes of antihypertensive agents. In the LIFE study showed that in the group of losartan compared with atenolol observed 13 % reduction in major cardiovascular events. In the losartan group had greater regression of LVH according to the ECG [173–175].

ARA has a comparable antihypertensive effect to ACE inhibitors with a proved high organ protective function [176]. Yusuf S. et al. showed that comparing ARA and ACE telmisartan was equivalent to ramipril in reducing BP, syncope and frequency of side effects [177].

Contraindications to ARA are the same as to ACE inhibitors except angioedema and combinations with ACE inhibitors [166].

According to the date [107], with the increase of frequency using ARA observed lengthening of the QTc interval by 8–13 % in patients with pacemaker. There are no researches on the effect of ARA in patients with AH and a pacemaker. In Mantziari L. et al. research was demonstrated that the use of the optimal dosage of the ARA was a condition of a favorable prognosis in patients with an implanted pacemaker and CRT [178].

CONCLUSION

The analysis of the literature has shown that despite the fact that cardiac pacing and CRT in the presence of possible solutions to the problem of arrhythmias and HF it does not cancel, but modifies the medical support of patients, which has been little studied.

As for the features of the medical control of AH in patients with a pacemaker and CRT, this question has not been practically studied, and the existing proposals do not go beyond existing recommendations for treatment in the general population.

The foregoing determines the exceptional relevance of studying the problem of drug control of AH in these patients.

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SIGNIFICANCE OF PULSE PRESSURE AND MANAGEMENT STRATEGY OF THE PETIENTS WITH PERMANENT CARDIAC PACING

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Clinical importance of the pulse pressure (PP) in patients with permanent pacemaker (PM) is discussed in this review. Clinical characteristics, hemodynamic parameters, stimulation parameters, depending on the PP, and the ability to optimize medication with antihypertensive drugs are considered. Implanted pacemaker and CRT are changing the PP, which substantiates the need for additional medical supervision.

KEY WORDS: cardiac pacing, cardiac resynchronization therapy, pulse pressure, drug therapy

ЗНАЧИМІСТЬ ПУЛЬСОВОГО АРТЕРІАЛЬНОГО ТИСКУ ТА МЕДИКАМЕНТОЗНА ПІДТРИМКА ПАЦІЄНТІВ З ПОСТІЙНОЮ ЕЛЕКТРОКАРДІОСТИМУЛЯЦІЄЮ

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В огляді обговорюється значення пульсового артеріального тиску (ПАД) у пацієнтів з імплантованим електрокардіостимулятором (ЕКС) і кардіоресинхронізуючою терапією (КРТ). Розглядаються клінічна характеристика, гемодинамічні показники, параметри стимуляції залежно від ПАД, а також можливість оптимізації медикаментозної терапії з використанням антигіпертензивних препаратів. ЕКС і КРТ змінює ПАД, що обґрунтовує необхідність додаткового медикаментозного контролю.

КЛЮЧОВІ СЛОВА: постійна електрокардіостимуляція, кардіоресинхронізуюча терапія, пульсовий артеріальний тиск

ЗНАЧИМОСТЬ ПУЛЬСОВОГО АРТЕРИАЛЬНОГО ДАВЛЕНИЯ И МЕДИКАМЕНТОЗНАЯ ПОДДЕРЖКА ПАЦИЕНТОВ С ПОСТОЯННОЙ ЭЛЕКТРОКАРДИОСТИМУЛЯЦИЕЙ

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В обзоре обсуждается значение пульсового артериального давления (ПАД) у пациентов с имплантированным электрокардиостимулятором (ЭКС) и кардиоресинхронизирующей терапией (КРТ). Рассматриваются клиническая характеристика, гемодинамические показатели, параметры стимуляции в зависимости от ПАД, а также возможность оптимизации медикаментозной терапии с использованием антигипертензивных препаратов. ЭКС и КРТ изменяет ПАД, что обосновывает необходимость дополнительного медикаментозного контроля.

КЛЮЧЕВЫЕ СЛОВА: постоянная электрокардиостимуляция, кардиоресинхронизирующая терапия, пульсовое артериальное давление, медикаментозная терапия

INTRODUCTION

Permanent cardiac pacing and cardiac resynchronization therapy (CRT) are the leading treatment methods of bradysystolic arrhythmias, as well as medical therapy resistant chronic heart failure (CHF) [1–2].

In 1985, the first pacemaker was implanted, and since then established as a highly effective method of bradyarrhythmias treatment. Permanent pacing reduces mortality, the number of admissions to hospitals, eliminates the symptoms of the disease and significantly improves the life quality (LQ), which is an additional goal of the treatment of patients with

bradyarrhythmias [1, 3]. The number of primary pacemaker implantations and replacements is increasing rapidly every year all over the world [4–5].

Both the first and the recent studies show that hemodynamics during pacing is associated not only with the general functions of the heart, but also with factors caused by the applied stimulation method [4].

5-letter code for a common nomenclature NBG-NASPE / BPEG stimulation that exists to describe the pacemaker programming since October 2001 was adopted. The first letter indicates the chamber paced (O – no, A – atria, the V – ventricle, D – dual chamber (A + V), S – single cardiac chamber (A or V)). The second letter indicates the chamber sensed (O – no, A – atria, V – ventricle, D – dual chambers, – single cardiac chamber). The third letter indicates how the pacemaker responds to a sensed event (O – no, T – trigger, I – suppression, D – indicates that there are dual modes of response (T + I)). The fourth letter indicates the possibility of programming (O – no, R – the pacemaker has rate modulation). The fifth letter specifies only the location or absence of multisite pacing, defined as stimulation sites in both atria, both ventricles, more than one stimulation site in any single chamber, or a combination of these (O – no, a – atria, V – ventricular, D – double function (A + V) [1].

The most common cause of pacemaker implantation is an AV block. The annual death rate from AV block before pacemakers' introduction into clinical practice reached more than 50 % [6]. Other indications for pacemaker implantation are sinus node dysfunction, chronic fascicular block, AV block associated with myocardial infarction (MI), hypersensitive carotid sinus syndrome [7], as well as for CRT in patients with CHF [1]. However, the indications for CRT are under discussion and development [8–10].

The important factor in the assessment of the clinical status of patients is the pulse pressure (PP) [11–14], which characterizes the work of the cardiovascular system, the degree of arteries walls tone and pumping function of the left ventricle (LV) [15–16]. Normal PP is considered to be 40–60 mm Hg, but not more than 60 % of the systolic blood pressure (SBP). Its value depends on the volume of blood that had accumulated during diastole and was ejected by the ventricle into the aorta in systole phase [17–18]. Another factor influencing the PP is the resistance encountered by the blood mass in the aorta during systole. PP has an important role in the regulation, because it reflects the blood volume pulse, while SBP and diastolic blood pressure (DBP) are its derivatives [19–21].

Changing of PP disrupts the normal blood supply to organs and tissues, increases the load on the heart and blood vessels, what is associated with decreasing of patients LQ, the progression of heart failure, the advent of life-threatening arrhythmias, increased complications of cardiovascular diseases (CVD) and sudden death in the world [22–27]. 54 % of adult deaths happen due to a stroke, and 47 % are associated with coronary heart disease (CHD) [28–31].

Low PP is associated with increased heart rate (HR) and is accompanied by rapid fatigue, weakness, dizziness and disorientation. Factors leading to such changes are: HF, aortic stenosis, hypovolemia, renal failure, pathology of adrenal and thyroid gland, trauma, accompanied by heavy bleeding, hypothermia, physical exertion [22, 32].

High PP is associated with a decreased HR and is accompanied by restlessness, agitation, anxiety, fear. Such conditions can be caused by stenosis or insufficiency of the aortic valve, atherosclerosis, increased intracranial pressure, endocarditis, anemia, hyperthyroidism [23–27, 33]. Increased PP with reduced DBP and insufficient blood filling of the coronary arteries are the cause of pain in the heart.

There are evidence of both the positive DDD and VVI [34], and the negative impact of AAI and DDD pacing modes on PP [35].

Multicenter studies indicate reduced risk of future development of HF and death, as well as the improvement of the clinical picture mostly in patients with PP > 40 mm Hg in one year after implantation of CRT-D [36]. However, high PP is associated with the development of CVD and death. It is necessary to pay attention to the impact of permanent pacemaker implantation and CRT on the various degrees of PP.

PP as a response function of neurohumoral control defines a new perspective for the analysis of the processes occurring in hemodynamics. In patients with implanted pacemaker and CRT heterogeneity PP requires careful selection of drug therapy and monitoring of its effectiveness.

1. CONDITIONS REQUIRING PACEMAKER IMPLANTATION AND PP

1.1. Acquired av block in patients with implanted pacemaker and pp

The frequency of the occurrence of AV blocks increases with age. The prevalence of I degree AV block is 0.45–5 % [37], in patients older than 60 years it is registered in 4,5–14,4 % of all cases; over 70 years – 40 %; after MI – in 8–13 %. The incidence of II degree AV block is – 9 %, III degree AV block reaches the maximum value in people older than 70 years [38] – in 2.5–8 % of patients with MI. The incidence of iatrogenic AV block is 0.5–3 % of all cases. According to WHO statistics, 17 % of sudden deaths due to acute HF occur due to the AV block. Most often, this pathology is diagnosed during a routine inspection by a physician or cardiologist. There are number of causes of AV block: diseases of ischemic, inflammatory, neoplastic and autoimmune nature. Heart defects, radiofrequency ablation, valve replacement, as well as drug intoxication can lead to rhythm disturbances [1].

AV block is anatomically divided into supra, intra- and infra-Hisian. I degree AV block is characterized by an abnormal PR-interval lengthening of more than 0.2 seconds and is usually asymptomatic. When PR interval is more than 0.3 sec (significant I degree AV block), it can cause symptoms due to catheter ablation of the fast path of AV connection with the continued conduction on a slow track. With such a blockade due to inadequate atrium contraction in the immediate vicinity of the ventricular systole, the hemodynamic consequences and symptoms similar to retrograde (ventricle-atrium) holding (pacemaker syndrome) may appear. Clinically manifested by shortness of breath, dizziness, palpitation, pulsation, and chest pain [6, 39–41]. When significant I degree AV block occurs, the atrium contraction comes prior to them complete filling, ventricular filling is impairing, pulmonary capillary pressure is increasing, stroke volume and end-diastolic pressure are increasing, that leads to increasing of PP. However, in the work of Alonso A., et al. PP associated with height of P wave, rather than with PR interval [42]. The reduction of symptoms and improvement in cardiac function is observed on the background of pacemaker implantation patients with PR interval > 0,3 sec by reducing of AV conducting time [39, 41]. Dual-chamber pacing with a shortened AV delay improves the condition of patients with long PR interval with LV dysfunction [43], and in some cases effect on the disappearance of orthostatic hypotension and indirectly normalizes PP [44].

II degree AV block Mobitz I is characterized by a progressive lengthening of the PR interval to the blocked contraction with a narrow QRS complex [45]. II degree AV block Mobitz II is characterized by a fixed PR-interval before and after the blocked complexes, usually associated with a wide QRS complex, and the damage of conducting occurs below the branch block trunk (on the background of the anterior-wall MI). In patients with II degree AV block of the first type hemodynamics worsens due to a loss of AV synchronization even without bradycardia. As the transition to an advanced AV block in this situation is not common, the stimulation is usually not indicated. An exception is the presence of severe symptoms – dizziness or syncope, chest pain if the block is associated with myocarditis or MI accompanied by SBP increasing, which indirectly indicates an increase in PP [6]. The second type of II degree AV block patients are often symptomatic, have a worse prognosis, often the progression to AV block of III degree is observed. Thus, the second type of II degree AV block and wide QRS complex shows diffuse lesion of the conduction system, and it is an indication for pacemaker implantation irrespective by symptoms.

In case of III degree AV block (complete blockage) AV dissociation occurs (no AV-conducting), and it is a sign of a serious organic lesion. An advanced II degree and complete AV blocks causes Morgagni-Adams-Stokes attacks, which are accompanied by HR slowing to 40 or less beats per minute (bpm), increasing PP, dizziness, weakness, darkening in eyes, loss of consciousness, pain in the heart. III degree AV block is the indication for pacemaker implantation. There are studies about the positive impact of DDD and VVI pacing modes in elderly patients with complete AV block, but with a single-chamber pacing a significant dilatation in the left atrium and decreased LV diastolic function is observed, which is an indirect effect on the reduction of PP [46–47].

In patients with AV block the reduction in frequency of symptoms of arterial hypertension (AH) is explained by the BP lowering during the 1 year observation period after pacemaker

implantation in the DDD/DDDR modes [48]. A slower decline in blood pressure (BP) in severe AH stage and grade is revealed. These indirectly show the PP decrease in patients with AV block and with DDD/DDDR pacing modes.

The survey [49] studied the influence of percent stimulation (< 10 % – group A, > 40 % – group B) on the structure and function of the heart in patients with AV block with a dual-chamber pacemaker. There are enlargements of atrium and LV and decreased ejection fraction (EF) in group B in comparison with the group A. There is indirect evidence of the growth of PP in patients with rhythm disturbances with increasing percentage of stimulation, which adversely affects the outcome of CVD.

In the study [50] in patients with AV block with VVI pacing mode during daily monitoring of BP an increase in PP by reducing ventricular pacing rate during the night is observed. The average level of PP is fixed at a constant frequency of ventricular stimulation during the day, but it is not a physiological decrease in BP during sleep, it is associated with an increased rate of target organ damage.

Presented publication of the PP changes after pacemaker implantation in patients with AV block are singular, and do not completely reflect the problem.

1.2. Bifascicular and trifasci-cular block in patients with implanted pacemaker and pp

The right bundle branch block (RBBB) can occur in healthy people, in anterior-wall MI and pulmonary embolism. The left leg bundle branch block (LBBB) is usually associated with the structural heart disease (CHD, CHF). The RBBB and LBBB predisposing factors include: atria septal defect, stenosis of the pulmonary artery, chronic obstructive pulmonary disease, aortic stenosis with calcification, cardiomyopathy, myocarditis, hyperkalemia, progressive muscular dystrophy, an overdose of drugs (quinidine, procainamide, strofantin), surgery and tumors of the heart, Lenegre Lev disease [51–52].

Bifascicular block is determined in electrocardiogram (ECG) as conduction disturbances below the AV node in two branches of RBBB or LBBB is determined. Trifascicular and alternating block are defined as a block of all three branches, either consecutively or at different times. Patients with such ECG changes and symptomatic advanced AV block have a high mortality rate and a significant incidence of sudden death [53–58].

Bundle branch blocks are usually asymptomatic because they do not cause changes in the HR, however patients with bifascicular block can have syncope [51, 59], due to decreased LVEF and increased end-diastolic pressure [60–61]. Increased SBP in patients with bifascicular and trifascicular block is observed [35]. These data indirectly indicates an increase of PP among patients in this group.

Electrophysiology study (EPS) can be useful in therapy assessment and selection for induced ventricular arrhythmias, which are often present in patients with bifascicular and trifascicular blocks, [1]. Meanwhile an increased risk of sudden death irrespective of the results of EPS is associated with syncope in patients with permanent or transient III degree AV block. Permanent pacing is indicated at bifascicular or trifascicular blocks if syncope of unclear genesis is present or used therapy may cause AV block, especially if the loss of consciousness are caused by transient III degree AV block [34]. Selecting of the pacing mode is performed the same way as in the AV block. Accordingly, the change of PP and its therapy at the given group are similar to the parameters in patients with an implanted pacemaker due to AV block.

Reduced SBP < 110 mm Hg correlates with a high risk of death and worsening HF in patients with an implanted pacemaker during the LBBB and moderate HF. Indirectly, the data indicate a decrease of PP in patients with LBBB and moderate HF. CRT reduces the risk of complications and increases the PP [62].

In the study [35] the daily monitoring of BP evaluated a decrease of PP in patients with bifascicular or trifascicular blocks, that is most by pronounced in the DDDR mode in late period after pacemaker implantation. However, there is an increasing of the PP at dual chamber pacing in DDD mode, in comparison with a single-chamber [34], which adversely influences the cardiovascular system function and an additional drug support is requires.

1.3. Sick sinus syndrome (sss) in patients with implanted pacemaker and pp

The dysfunction of sinoatrial (SA) node disturbs the frequency of atria contractions, what causes pathological bradycardia, asystolic pause and increases PP [63]. The incidence of the SSS is less than 0.2 % [64]. There are

internal and external factors that can cause SA node dysfunction: CHD or MI, AH, systemic diseases of connective tissue, endocrine disorders, neuromuscular disease, surgical injuries [64–65].

Paroxysmal tachycardia on the background of SSS can occur in some patients [66]. Therefore, patients experience a permanent emotional stress in addition to disturbances of hemodynamics during the paroxysms. This leads to the decreasing of LQ and manifests by disability, faintness, fatigue, circulation insufficiency events, memory impairment [67]. 17-year study [68] that involved 213 patients with SSS, shows a high risk of sudden death, HF, stroke, atrial fibrillation (AF) and requires a permanent pacemaker implantation. Increasing of the BP is also associated with the SSS, which indirectly influences on increase of the PP in the current pathology.

There are indications for the pacemaker implantation: SSS with documented symptomatic bradycardia or pauses, clinically manifested by chronotropic incompetence; symptomatic sinus bradycardia as a result of long-term drug therapy, which cannot be discontinued or replaced with another treatment; syncope of the unknown origin, when major deviations from the normal function of the SN identified or provoked by the EPS [1]. AV stimulation, combined with pacemaker settings that minimize ventricular pacing is the optimal strategy for the treatment of SSS [1, 69]. It improves LQ, reduces cardiovascular and total mortality and incidence of AF [70], reduces thromboembolic complications and pacemaker syndrome events which associated with loss of AV synchrony and manifests by weakness, dizziness, syncope, followed by decreasing of the myocardium contractile function [71].

We found only one study [72], where in patients with SSS the increase of cardiac productivity is observed on a background of atrium pacing, which leads to increase of cardiac index up 30%, stroke volume by 15% and decrease of preload. However, there is an increase of PP (59,2 ± 2,3 mm Hg) Despite the improvement in hemodynamics. There is a decrease of cardiac productivity on the background of ventricular pacing, thereby there is a decrease of cardiac index and stroke volume by 15–20 %, increase of preload and decrease of PP (54,3 ± 2,2 mm Hg).

1.4. Carotid sinus syndrome (css) and neurocardiogenic syncope in patients with implanted pacemaker and pp

CSS is manifested by syncope or presyncope as a response to carotid sinus stimulation due to its high sensitivity [73]. The data [74] indicate that the syncope is common in all age groups with the peaks in adolescence and elderly. The recurrence rate of syncope increases linearly from 0.3 % during 30 days to 22 % within two years of observation. The mortality rate for one year varies between 5.7 and 15.5 %. Most of syncopes of unclear genesis are caused by a CSS in elderly patients. Passive orthostatic test (head-up tilt-table testing) is used for the diagnostics of neurocardiogenic syncope [75–76]. Before the test all cardio- and vasoactive drugs should be canceled. Duration of the test is 45 minutes or until syncope develops. Neurocardiogenic syncope is classified by ECG data in the three leads and by BP data [77–78]:

– mixed type: duration ≤ 10 seconds, HR ≤ 40 bpm, the absence of asystole > 3 sec, lowering of BP precedes the HR reduction;

– cardioinhibitory type: duration > 10 seconds, HR > 40 bpm, the absence of asystole > 3 sec, lowering of BP precedes the HR reduction;

– cardioinhibitory type with asystole: the lack of asystole > 3 seconds, hypotension (decreasing of SBP to 80 mm Hg) with decreasing in HR at the same time;

– vasodepressor type: HR ≥ 10 % from baseline when syncope is present, a significant decrease of the SBP.

The significant decrease of SBP and slight decrease of DBP are indirectly associated with reduction of the PP in patients with CSS [75, 79].

The indications for pacemaker implantation are recurrent syncope caused by carotid sinus stimulation in patients who needs a minimal pressure on the area of the carotid sinus to cause episodes of ventricular asystole > 6 sec duration in the absence of drugs depressing SN function or slowing AV conduct.

The study [80], which includes 138 elderly patients with the CSS, history of syncope and positive tilt-table testing in 67.4 % of cases showed that pacemaker implantation completely suppresses the symptoms in 83.3 % of cases. However symptoms remain unchanged in 10.9 % of the mixed CSS that is associated with preservation of vasodepressor

component. There is indirect evidence that the pacemaker implantation did not normalize PP in patients with vasodepressor type of CSS in comparison with cardioinhibitory type.

1.5. Hypertrophic cardiomyopathy (hcm) and neurocardiogenic syncope in patients with implanted pacemaker and pp

HCM is a genetic CVD of the myocardium, characterized by local ventricular hypertrophy, diastolic dysfunction and the development of arrhythmias [81]. The incidence of HCM is 1 in 500 people worldwide [82–84]. Factors that increase the sudden death in these patients, include: heredity, the presence of syncope, severe LV hypertrophy or obstruction of the LV outflow tract on echocardiography, abnormal BP response to exercise [81].

The study [85] presents a clinical case of a patient with apical HCM, CAD and AH. His PP is 56 mm Hg and HR is 50 bpm during the rest. During the exercise test PP decreases to 32 mm Hg and HR increases to 162 bpm. Multicenter study [86] indicates that the decreasing of the SBP up to 10 mm Hg and indirect decreasing of the PP during physical exertion is an independent factor for the development of CVD and increased mortality.

Clinically HCM is manifested by shortness of breath, weakness, chest pain, syncope, arrhythmias (tachycardia, bradyarrhythmia, AF, front and LBBB).

Implantation of the defibrillator and dual chambers synchronized AV-stimulation are invasive methods of HCM treatment in patients with high risk of sudden death [1]. Pacemaker reduces the frequency of myectomy application, alcohol ablation, and reduces the risk of sudden death [87–89]. Dual-chamber pacing mode with a short AV delay improves hemodynamics when outflow tract obstruction is present by restoring the sequence of LV excitation, which provides an increase in the diameter and volume of outflow tract and reduction of LV obstruction, increase of SAP and indirectly increases PP.

In end-stage HCM for relieving HF symptoms CRT is recommended [1]. LV and left atria reverse remodeling are present in this group of patients [90] that improves hemodynamic and indirectly increases the PP.

Schinkel A.F. et al. [91] studied 2190 patients with HCM, syncope (41 %), reduced PP during exercise (25%), LV hypertrophy (20 %) and unstable ventricular tachycardia (46 %). One year after the implantation of CRT the cardiac mortality is reduced to 0.6 % in this group of patients.

1.6. Chf in patients with implanted pacemaker and pp

The prevalence of CHF is 1–2 % in the population and it increases to 10 % in elderly patients [92]. Mortality is 20 % among those who is under 75 years old and 40 % – over 75 years [1]. Currently, HF is classified according to the LVEF: systolic HF with reduced EF (< 45–50 %) and diastolic HF with preserved EF. CAD and MI are associated with systolic HF, and AH and diabetes – with diastolic HF [93–95]. CHF characterized by a decrease in LQ, social and psychological consequences. Clinically it is characterized by shortness of breath, fatigue and reduced physical activity. Tachycardia, tachypnea, decrease of the EF, low SBP and PP indicates a poor prognosis and advanced stage of the CHF [94, 96]. Biton Y. et al. show that the increase of the PP ≥ 75 mm Hg in response to exercise has a more favorable outcomes for systolic HF and the PP <75 mm Hg increases the risk of death in this case [62].

There are evidence of low PP association with high risk of cardiovascular complications and increased mortality in patients with II-IV functional classes of HF, after myocardial MI [62, 97].

In a study [36] it is demonstrated that low PP is associated with a worse outcome in hospitalized patients with systolic HF, however when PP > 40 mm Hg the opposite LV remodeling occurs by reducing of LV end-systolic volume.

There are indications for CRT: III-IV functional class (FC) of HF in patients with sinus rhythm, the QRS duration ≥ 120 ms and EF ≤ 35 %; III-IV FC of HF with the duration of the QRS ≥ 150 ms and EF ≤ 35 %; II FC of HF in sinus rhythm, the QRS duration ≥ 120–130 ms and EF ≤ 30–40 %; with QRS complex duration ≥ 150 ms, EF ≤ 30 % [1]. There are indications for CRT in patients with a permanent or long-term persistent AF: III-IV FC of CHF with QRS complex duration ≥ 120 ms EF ≤ 35 %, with the holding AV ablation in patients with a rare ventricular rate (lesser than 60 per minute at rest and lesser than 90 per min under a load).

In the study [98] in 1177 patients with systolic HF the effect of CRT-D and pacemaker

is compared. It is noted that the CRT-D implantation, EF < 35 % and the QRS complex duration ≤ 130 ms are associated with a high mortality, as compared to the pacemaker.

CRT increases exercise tolerance, blood oxygen saturation, and improves LQ, reduces re-hospitalization and mortality due to HF [72, 77], helps to restore the myocardial contraction synchrony, improves the contractility of the LV and leads to the LV reverse remodeling, what increasing LVEF. It is accompanied by PP normalization [36, 62].

The study [36] observes that the positive echocardiographic response occurs when PP > 40 mm Hg for one year after implantation of CRT-D in patients with systolic HF. Also in this group, the risk of HF development and death reduces on 50 % in comparison with a low-PP group (<40 mm Hg).

There is an increase of SBP on 8.5 mm Hg in 15 patients with III-IV FC CHF with EF < 40 %, QRS complex duration ≥ 125 ms after using biventricular CRT in combination with right ventricular stimulation [99]. It indirectly indicates an increase of the PP in this type of stimulation.

2. MEDICAMENT SUPPLEMENT OF PATIENTS WITH IMPLANTED ECS AND PP

The contemporary implantable ECS as well as CRT are high technological complex and programmed devices for arrhythmias prevention and execution of algorhythms for reduction of right ventricular stimulation and ultimately, for elevation of LQ and mortality reduction in cardiovascular pathology [1].

A constant control of ECS work and of the state of CRT is required and aimed to reveal some diagnostic and corrective mistakes in their work with the following optimization of the program for achievement of the best clinical effect and prolongation of devices' service terms as well as for resolution of the problem of management [2, 100]. The first programmation of the device is carried out directly during the operation and then on the following 3rd and 7th days. In 6–12 weeks after implantation a chronic threshold of stimulation is formed. The thresholds of stimulation should be checked in this period and if it is necessary. To be regulated. On the 6th and 12th months after operation the correction of ECS work is controlled. Again and in the future if there are no complaints of the patient the latter is observed once a year. An important task is also an evaluation of the battery work and when its exhaustion is revealed the battery should be replaced [101].

ECS and CRT don't always decrease a frequency of recurrent hospitalizations and fatal outcomes [102]. In this case an additional medicament supplement is not abolished. A usage of some groups of medications and decrease of PP in a different degree influence on the reduction of the risk of cardiovascular complications [103]. Some of the drugs, such as beta-adrenoblockers (BAB), calcium channel blockers (CCB), chinidine, aimaline, isuprel, isadrine are capable to increase of ECS threshold and on the contrary, such agents as prednisolone, norepinephrine, and ephedrine are able to decrease of ECS threshold [104–106].

It should be noted that the action of the drugs influenced on the variability of PP in patients with implanted ECS or performed CRT is not enough elucidated in the contemporary literature.

2.1. Diuretics in patients with implanted ecs and pp

Although in patients with implanted ECS diuretics don't change PP, but some agents of this group of drugs prescribed to hypertensive patients can decrease it. So, in patients with isolated systolic AH indapamide decreases risk of cardiovascular complications due to reduction of PP < 60 mm Hg [107].

The ASPIRANT study [108] demonstrated that spironolactone was less effective in reduction of PP in patients with AH and initial DBP over 97 mm Hg. In patients with resistant AH the contribution of spironolactone (25–50 mg daily) to reduction of PP realizes in 12 weeks of therapy due to decrease in SBP be 8.7 mm Hg (the PATHWAY-2 study) [109].

By analogy, a loop diuretic furosemide (40–60 mg daily) in persons with AH compared to placebo in 8.8 weeks of treatment can decrease PP due to more marked reduction of SBP (by 8 mm Hg) then of DBP (by 4 mm Hg) [110].

High doses of furosemide (over 80 mg daily) in patients aged older 60 years with CHF of III-IV FC, LVEF ≤ 35 %, QRS duration ≥ 120 ms and LBBB or RBBB are shown to increase a risk of cardiovascular mortality probably due to PP growth. So, before CRT and high daily doses of furosemide an average PP was 45 mm Hg and then in a year after CRT and furosemide therapy there was a decrease in PP

to 39.6 mm Hg but two years later the further more marked growth of PP to 51.8 mm Hg was observed [111].

The MADIT-CRT study has shown a negative effect of diuretics on the course of CHF in patients with CRT developed in an increase of frequency of hospitalization and complications. However torasemide administration could improve a clinical picture in such patients [112].

2.2. Bab in patients with implanted ecs and pp

The influence of nebivolol in patients aged older 70 years with CHF was studied depending on initial BP after CRT. Prescription of nebivolol 2.5–5–10 mg daily compared with placebo was discovered to decrease PP by 1.5 mm Hg (PP was 56.4 mm Hg in the group of treatment vs 57.9 mm Hg in placebo group). However even such insignificant PP reduction in patients with CHF after CRT diminishes development of cardiovascular complications and mortality [113].

Combination of BAB with angiotensin converting enzyme (ACE) inhibitors in patients with CHF and hypertensive CSS positively influenced on the further clinical outcome [114–115], the best outcome after CRT is observed at high doses of antihypertensive agents [116]. In patients with dual chambered ECS carvedilol 6.25 mg daily promotes a reduction of PP be 10 mm Hg due to positive influence on SBP [105].

In 18 % of patients with SSS a usage of BAB after implantation of dual chambered ECS is associated with development of the 2nd and 3rd degree AV block [117].

BAB is used in the treatment of ECS and CRT-induced arrhythmias of supraventricular and ventricular origin. Prescription of BAB to the patients with CHF after implantation of ECS or executed CRT in decreased a risk of ECS' complications [112, 118–119]. Alongside with a prolongation of QRS complex' duration a frequency of BAB prescription was found out to be grown [120].

In patients without arrhythmias induced by ECS and CRT, BAB is used in small daily doses due to a growth of frequency of unfavorable outcomes and hospitalizations [121].

2.3. Ccb in patients with implanted ecs and pp

Amlodipine as one of the hypotensive agents can be used for reduction of PP in patients with implanted ECS. It has been noted a reliable decrease in PP by 5.1 mm Hg without change of HR in such patients already in 8 weeks of treatment with amlodipine 10 mg daily [122].

A tendency to elevation of the threshold of ECS without an influence on with verapamil 240 mg daily in 2 months of treatment in patients with supraventricular tachyarrhythmia or AF and implanted DDDR ECS HR is discovered [123].

Higher velocity of coronary flow was revealed in treatment with verapamil compared with its withdrawal in patients with HCM. The endothelium depended vasodilatation is known to be impaired in such patients and therapy with verapamil promotes a restoration of vasodilatation response in the conditions of stress associated with ECS [124].

2.4. The inhibitors of ace, antagonists of angiotensine ii receptors (aar ii) in patients with implanted ecs and pp

Administration of ACE inhibitors or AAR II in patients with CHF in CRT leads to long term favorable outcomes. These groups of agents improve prognosis in CRT in cases of their usage in optimal daily doses [125].

Lisinopril 2.5 mg daily combined with BAB, diuretic, acetylsalicylic acid and digoxin is reported to improve a total state of patients with performed CRT due to CHF and constant form of AF [105]. Therapy with lisinopril is occurred to reduce PP resulted in SBP decrease by 10 mm Hg after 14 months of treatment.

Right ventricular ECS can evoke a ventricular dyssynchrony, aggravate cardiac output and increase a PP [49]. In patients with full AV block and dual chambered ECS a usage of ACE inhibitors decrease a frequency of hospitalizations and cardiovascular complications.

CONCLUSION

PP is an independent predisposing and prognostic factor for cardiovascular complications and mortality, and therefore is being intensively studied.

The implantation of pacemaker and CRT, solves the problem of bradysystolic arrhythmias and HF, and leads to regular changes in PP among the other hemodynamic parameters. The PP role and abilities of its optimization, including due to medical management of patients, is still not studied appropriately.

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