The research of parameters of cardiac rythm variability of arterial hypertension in children and adolescents

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ABSTRACT

Currently both the definition of some measures with a strategic significance concerning the physiological state of the human body and some ways of mortality prevention caused by cardiovascular diseases in children and adolescents are considered of a great importance, constituting morbidity and mortality major problem in population worldwide. In order to solve these tasks different specialists in cardiology have initiated for decades researches in etiopathogenesis and pathophysiology of chronic heart failure.

In recent years more frequently the fact that heart failure is a complex disorder with progressive evolution, characterized by structure and cardiac function damage is emphasized, the endogenous neurohormonal activation plays a significant role. The primary role in triggering heart failure in children refers to chronic myocardial dysfunctions which constantly maintains morbidity at a high incidence due to cardiovascular diseases.

***Aim.** Indices evaluation of heart rate variability in chronic myocardial dysfunctions in children and adolescents secondary to arterial hypertension.*

***Material and methods.** A number of 137 children were included in the study, from these 52 patients having arterial complicated hypertension and chronic heart failure were selected, who showed signs of chronic dysfunctions of the myocardium according to the investigational data, forming the core group, and 85 healthy children without any signs of heart failure who formed the control group. On the basis of instrumental exploration the diagnosis confirmation of chronic myocardial dysfunctions was established exerting the following optional methods: (a) ECG performed at Cardman apparatus Fx-3264 (Japan); (b) EchoCG Doppler; (c) x-ray test of the thoracic cavity's organs, ECG computerized monitoring at the outpatient department according to Holter's method, as well as TA computerized monitoring at the outpatient department in 24 hours.*

***Results.** Electrophysiological changes in patients with arterial hypertension demonstrated the presence of electrocardiographic signs typical of chronic myocardial dysfunctions, such as sinus tachycardia in 63.5% of cases, sinus bradycardia in 3.8% of cases, changes in QRS morphology in 88.5% of cases, supraventricular extrasystole in 11.5% of cases, ventricular extrasystole in 11.5% of cases, abnormal repolarization processes in the left ventricle in 94.2% of cases, signs of left ventricular myocardial hypertrophy in 61.5% of cases. One of the myocardium remodeling predictors is considered myocardium hypertrophy of the left ventricle being determined in patients with significant arterial hypertension among groups ($p<0.01$).*

The dynamic group analysis' result of the heart rate variability in patients with arterial hypertension after a thorough check up of the main ECG events, the time parameters have been determined automatically as: SDNN, SDNNi, SDANN, r-MSSD, pNN50 that noted significantly increased values compared with the control group at inclusion in the study phase and the spectral ones that also showed conclusive increases versus the control group. Dynamic evaluation of these parameters showed irregular oscillations, the values being significantly increased compared with the control group, confirming the result of metabolic distur-

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bances that occur after myocardial hypoxia processes being the cause of changes in cardiac electrophysiology in chronic myocardial dysfunctions.

Conclusions. 1. *Due to the results of this study we established that in the followed up children and adolescents with arterial hypertension changes in cardiac electrophysiology occurred that were defined both by the occurrence of heart rhythm disorders such as sinus tachycardia in 63.5%of cases, sinus bradycardia in 3 8% of cases, changes in QRS morphology in 88,.5% of cases, supraventricular extrasystoles in 11.5% of cases, ventricular extrasystole in 11.5% of cases, abnormal remodelling processes in the left ventricle in 94.2% of cases, hypertrophy signs of left ventricular myocardium in 61.5% of cases.* **2.** *In the patients examined in this study significant changes in heart rate variability parameters were determined, which denote a disorder of regulatory systems in cardiac electrophysiology and significantly influences the clinical condition of patients and the development of chronic myocardium dysfunctions. The heart rate variability parameters modifications' specifics in chronic heart failure secondary to arterial hypertension influences the prognosis of patients with an increased risk of sudden death.*

Keywords: chronic myocrdial dysfunction, arterial hypertension, biomarkers, myoglobin, troponin I, C reactive protein, myocardial remodeling

INTRODUCTION

Currently both the definition of some measures with a strategic significance concerning the physiological state of the human body and some ways of mortality prevention caused by cardiovascular diseases in children and adolescents are considered of a great importance, constituting morbidity and mortality major problem in population worldwide. In order to solve these tasks different specialists in cardiology have initiated for decades researches in etiopathogenesis and pathophysiology of chronic heart failure (1). In recent years more frequently the fact that heart failure is a complex disorder with progressive evolution, characterized by structure and cardiac function damage is emphasized, the endogenous neurohormonal activation plays a significant role.

The primary role in triggering heart failure in children refers to chronic myocardial dysfunctions which constantly maintains morbidity at a high incidence due to cardiovascular diseases (2). At the age of a child, the triggering causes of chronic myocardial dysfunctions can be both congenital cardiopathies, and idiopathic inflammatory heart disorders such as bacterial endocarditis, myocarditis, dilated, hypertrophic cardiomyopathies, pericarditis, various valvular pathologies, cardiac rhythm and management disorders , as well as high blood pressure (3-5).

In chronic myocardial dysfunctions the pathogenetic mechanisms are not yet fully deciphered, but certainly comes the muscular fiber excessive charging with calcium, as well as the decrease of the contractile protein synthesis level, both effects having consequently continued deterioration of the myocardial contractility. An essential role in realizing the hemodynamic compensatory mechanisms that are included in heart failure is offered both to neurohormonal hyperactivation, especially of the sympatho-adrenergic system and the renin-angiotensin-aldosterone system and natriuretic peptide. In fundamental researches, the neurohormonal activation impact and cytokines influence in the installation and progredience of chronic heart failure syndrome were proved.

The negative consequence of neurohormonal activation in chronic myocardial dysfunctions present sympathetic activation, whether it is manifested by increased levels of serum catecholamines or by increased cardiac sympathetic activity and has a direct toxic effect on the heart muscle, these fundamental mechanisms have been confirmed in classical clinical studies (6,7).

STUDY OBJECTIVES

The estimation of electrocardiographic parameters modifications in the development of arterial hypertension in children and adolescents. The evaluation indices of heart rate variability in chronic myocardial dysfunctions in children and adolescents.

MATERIAL AND METHODS

Steps to initiate researches focused on the creation and completion of a clinical questionnaire, which included information gathered about 250 anamnestic, clinical, investigational and healing indicators were estimated complexly. Thus, the total number of patients included in the study was of 137 children, from these 52 patients with arterial complicated hypertension with chronic heart failure were selected, who

according to the investigational data showed signs of chronic dysfunctions of the myocardium and formed the basic group and 85 healthy children without any signs of heart failure who formed the control group. The study sample was divided into two groups of research the 1st group of research included 26 patients with CHF secondary to arterial hypertension, who received treatment with Captopril and Spironolactone, mean age 14.48 ± 0.37 years; the 2nd group study consisting of 26 patients with average age of 14.59 ± 0.42 years, with chronic heart failure secondary to arterial hypertension they were administered Enalapril in the dosage of 0.06 mg / kg / every 24 hours once a day. In the present study a special investigational programme was used for each patient its exertion allowed to put the clinical diagnosis. The treatment of patients included in the study was initiated only in the inpatient department with prompt monitoring clinical, hemodynamic indicators, including the values of heart rate, pulse, blood pressure, urine output. The duration of treatment in these patients is individually programmed according to preparation tolerance, improving the clinical, hemodynamic indicators, regression of chronic heart failure clinical signs, improving exercise tolerance as well as biochemical and hormonal indices normalization. Clinical data were objectified by the support of laboratory, ECG and echocardiography investigations. Based on the instrumental exploration the diagnosis confirmation of chronic myocardial dysfunctions was found exerting the following optional methods: (a) ECG was performed at Cardman apparatus Fx-3264 (Japan), (b) EchoCG, (c) chest organs radiology with calculation of the cardiothoracic index, ECG computerized monitoring in the outpatient department according to Holter method at Astro-Card apparatus (2000) as well as TA computerized monitoring in the outpatient department in 24 hours. During the ECG examination heart rhythm disorders were determined both at the computerized and ectopic centers, remodeling process of left ventricular myocardium (especially in the ST segment and T wave), ventricular electrical systole extension – QT interval >360 ms, signs of hyperfunction and/or hypertrophy of the LV myocardium.

The program of the study included assessment of heart rate variability in patients with chronic myocardial dysfunction secondary to hypertension automatic ECG recording time 24 hours after the Holter method for each patient.

Analyzing Holter's records, after a thorough editing of the main ECG events, the following indicators of frequency heart rate were automatically received during the analysis period: average frequency of cardiac contractions (FCC) in 24 hours, maximum FCC in 24 hours evidence, calculated for five identical RR intervals of sinus origin, FCC minimum sinus rhythm within 24 hours of evidence, calculated on five identical RR intervals of sinus origin. Heart rate variability analysis, performed within 24 hours of time, included assessment of the following parameters: NN med – the RR intervals' average of sinus origin (NN) for the whole period of research; SDNN – standard deviation of NN intervals; SDANN - NN average standard deviation within 5 min of time; SDNN index – average within 24 hours of NN for the standard deviation within 5 min; rMSSD – square root of the sum of square differences in NN intervals during 24 hours; pNN50 – is the ratio of NN intervals, different from the previous ones by way of 50 ms duration, expressed in percentages, for the total number of NN intervals. Except for pNN50 all time parameters were assessed in absolute ms values. Spectral analysis of variability of cardiac rhythm (VCR), carried out in 24-hours interval included arranging a number of NN intervals that reflect the dependence of values of time intervals NN – NN (t). In such a way the time (t) management was equal to 0.5 sec. If artifacts or extrasystolic complex were met then the previous or next RR intervals were excluded from the analysis and NN interval current value were calculated by linear interpolation method. The quantitative characters of different parts of the NN spectrum were assessed: total spectral power (1.15 × 10 - 5 to 0.40 Гц) - TotP, NN undulations' power in the range of ultralow frequencies (0.0033 to 0.04 Гц) – VLFP, undulations' power low frequency ranging from (.04 to .15 Гц) – LFP, NN undulations' power ripple in the range of high frequencies (0.15 to 0.40 Гц) - HFP.

Calculations were performed in absolute power (мs²) with subsequent improvement of the linear values (мs) by excluding thesquare root. Heart rate variability indices were grouped according to the range of variations of the reflected NN intervals. The heart rate variability parameters with ultralow frequency were noted – SDNN, SDANN, TotP and ULFP, and to the low frequency parameters were related - SDNNi, VLFP and LFP and for those with high frequency – rMSSD, pNN50 and HFP. The program of study included heart rate variability parameters – time parameters: SDNN, SDNNi, r-MSSD, pNN50 and spectral parameters: total power (ms²), low frequency power (ms²) and high frequency power (ms²).

RESULTS

In order to diagnose left ventricle myocardial hypertrophy (LVH) the following methods were used: ECG and echocardiographic. For ECG interpretation in children it's always necessary to take into account the child's age. Estimation of LVH signs is performed in chest derivations. The electrical axis positioning with deviation to the left points out the left ventricle myocardial hypertrophy. Signs suggestive of LV myocardial hypertrophy are - R-wave amplitude in V6 bypass is higher than the norm by age; S wave in V1 bypass is deeper than norm for age; deep Q waves in thoracic derivations. LV myocardial hypertrophy criteria after ECG data are: Sokolov - Lyon sign [S (V1) + R (V5 or V6)]> 38 mm, where S (V1) – voltage S in V1; R (V5 or V6) R voltage in V1 and V6 derivations. It should be noted that the sensitivity of ECG method for assessing LV myocardial hypertrophy is not absolute, because the ECG criteria are indications of voltage and QRS duration complex, although these indicators depend on age, sex, constitutional type, which is important for pediatric ages. During investigations electrocardiographic changes in patients with arterial hypertension were determined in corresponding groups whose characteristics are shown in Table 1.

Comparative analysis of electrocardiographic abnormalities at an early stage in patients with arterial hypertension showed conclusive true differences by the presence of electrocardiographic signs typical of chronic myocardial dysfunctions, such as changes in the QRS pattern and T wave, including suggestive signs of disturbances remodeling processes – various changes of ST-T and QT prolongation interval up to 40-42". One of the predictors of cardiac remodeling is considered left ventricle myocardium hypertrophy which has been determined in patients with significant arterial hypertension among groups (p <0.01). Totally per group we recorded sinus rhythm in 98% of cases, sinus tachycardia in 63.5% of cases, sinus bradycardia in 3.8% of cases, changes in QRS morphology in 88.5% of cases, supraventricular extrasystole in 11.5% of cases, ventricular extrasystole in 11.5% of cases, abnormal remodeling processes in the left ventricle in 94.2% of cases, signs of left ventricular myocardial hypertrophy in 61.5% of cases. Electrophysiological signs documented by ECG examination in observational dynamics in patients from the studied groups are shown in Table 2.

After the data presented in the table in patients with chronic myocardial dysfunctions secondary to arterial hypertension improvements in generating heart rate are marked returning to sinus rhythm in 100% cases, reducing sinus tachycardia in 57% cases of QT interval duration 27.7 ms, QRST complex morphology improvement in 73% of cases, supraventricular extrasystole disappearance and reduction of the frequency of ventricular extrasystole in 10% of cases, improvement in LV myocardium remodeling processes in 89% of cases and reduction of myocardial remodeling of LV hypertrophy in 54% of cases.

To estimate homeokinesis in the majority of patients with chronic myocardial dysfunctions secondary to arterial hypertension vegetative dysfunctions of different variant and degree of clinical expression were assessed. To evaluate the primary vegetative tonus the cardiointervalography was performed due to which various types of vegetative dysfunctions were determined.

TABLE 1. *Electrocardiographic signs characteristics at an early stage in patients with chronic myocardial dysfunctions secondary to arterial hypertension*

ECG Signs	I study group (n = 26)		II study group (n = 26)		p
	N	%	N	%	
ECG signs – Sinuses rhythm	26	100	25	98.07	>0.05
Sinuses tahicardia	16	61.5	17	65.3	>0.05
Sinuses bradicardia	1	3.8	1	3.8	>0.05
Q-T, ms Interval duration	368.2±11.2		386.3±10.2		>0.05
Segm. ST, mm depression	1.0±0.10		1.2±0.06		>0.05
Morphology modifications signs compl. QRST	26	100	20	76.9	<0.001
Extrasystole, ventricular/s	4	15.3	2	7.6	>0.05
Ventricular extrasystole	2	7.6	4	15.3	>0.05
Remodelling dysfunctions in LV myocardium	26	100	23	88.4	<0.05
HVS signs	21	80.7	11	42.3	<0.01

Note*. Statistically significant differences between groups – * p <0.05, ** p <0.01, *** p <0.001*

TABLE 2. *Evolutionary characteristics of electrocardiographic signs in patients with chronic myocardial dysfunctions secondary to arterial hypertension*

ECG signs	Study group (n = 52) initial		Study group (n = 52) Over 6 months		p
	N	%	N	%	
ECG signs – Sinuses rhythm	51	98.07	52	100	>0.05
Sinuses tahicardia	33	63.4	3	5.8	<0.001
Sinuses bradicardia	2	3.8	0	0	<0.05
Q-T, ms Interval duration	382.3±13.2		354.6±8.4		>0.05
Segm. ST, mm depression	1.10±0.06		0.6±0.02		<0.001
Morphology modifications signs compl. QRST	46	88,4	8	15.4	<0.001
Extrasystole, ventricular/s	6	11.5	1	1.9	<0.05
Ventricular extrasystole	6	11.5	0	0	<0.001
Remodelling dysfunctions in LV myocardium	49	94.2	3	5.8	<0.001
HVS signs	32	61.5	4	7.7	<0.001

Note: *Statistically significant differences between groups – * p <0.05, ** p <0.01, *** p <0.001*

According to cardiointervalography data the vegetative reactivity of hyperyimpathicotonic type was determined in 48 patients (92.3%) whose clinical manifestations were expressed by pale skin and reduced moistureof the skin, white dermographism, dilated pupils. The vegetative asympathicotonic reactivity was determined in 4 patients (7.6%). Vagotonia was not assessed in this group of patients. From these data resides the fact that the higher the initial autonomic tone, less reservations of vegetative reactivity which corresponds to main law in vegetology. In the general group of patients with chronic heart failure secondary to arterial hypertension the indices of heart rate variability were appreciated that are considered as the main estimation electrophysiological elements of life prognosis and myocardium chronic dysfunctions evolution. From the speciality findings it is known that arterial hypertension syndrome in these patients is associated with the increased risk of morbidity and mortality rate.

Parameters estimation of heart rate variability in both groups with arterial hypertension at the initial stage of patients' inclusion in the study are reflected in Table 3.

Based on vegetative reactivity differentiation after cardiointervalography, within Holter monitoring we initiated the analysis of heart rate variability indices assessing the low-frequency parameters (SDNNi) and ultralow (SDNN and SDANN) which manifested authentic initially increased values and in dynamic observation compared with the similar values in the control group.

The characteristics of changes of high frequency parameters – rMSSD, pNN50 and HF the conclusive increased values in patients with arterial hypertension compared with control group was also specified. Comparative estimation of the parameters of heart rate variability had the following specificities: time parameters with ultralow frequency, particularly SDNN noted values increase compared with the control group by 23% in group I and 34% in group II at the stage of inclusion in the study with oscillatory variations of reduction study over 6 months for group I with 4% and 20% for group II. The values of time parameter with ultralow frequency - initially SDANN noted conclusive differences compared with the control group by 75% in group I and in group II by 84%, after 6 months in group I SDANN values decreased by 13% and group II by 22%. Heart rate variability parameter SDNNi with low frequency initially had conclusive changes by 29% in group I and 25% in group II, but in six months there is a 5% reduction in SDNN value in group I, while in group II there is a negative trend with an increase of 22%. Parameters of high frequency heart rate variability – rMSSD, pNN50 and HF, estimated in automatic Holter ECG monitoring in 24 hours, also had accurate changes to the control group. The time parameter r-MSSD noted an elevation of initial value in group I to 86% and in group II to 72% compared to the control group, while the dynamics is assessed up to 8% increase from initial value in the first group and a reduction of 12% in group II of study. Specifics of parameter changes with high pNN50 frequency heart rate variability indicates initially an increase up to 55% in both groups compared to the control group with no changes in the group dynamics of group I media and group II reduction in value by 26%. HF parameter changes initially were virtually identical for both groups and accounted 60% compared with the control group, with a

TABLE 3. *Comparative characteristics of heart rate variability under the influence of Captopril and Spironolactone versus Enalapril therapy in patients with chronic myocardial dysfunction secondary to arterial hypertension*

Index	I Initial Study Group (n=26)	I Study Group 6 months (n=26)	II Initial Study Group (n=26)	II Study Group 6 months (n=26)
Control	84,5±3,4 (100%)			
FCC med	82,0 ±2,3 (97%)	76,4±1,2* (90%)	79,3 ±1,2 (94%)	75,0±1,3** (89%)
p	p<0,05		p<0,05	
Control	168,3±10,2 (100%)			
SDNN (ms)	207,5±10,6** (123%)	201,4±8,0* (119%)	226,0±10,4*** (134%)	193,8±10,9 (114%)
P	p>0,05		p<0,05	
Control	89,1±6,2 (100%)			
SDNNi (ms)	115,5±5,3** (129%)	111,5±4,0** (124%)	112,3±6,0** (125%)	131,7±13,6** (147%)
P	p>0,05		p>0,05	
Control	108,6±8,5 (100%)			
SDANN (ms)	189,4±9,0*** (175%)	175,9±7,4*** (162%)	199,0±8,6*** (184%)	176,3±9,1*** (162%)
P	p>0,05		p>0,05	
Control	58,11±8,8 (100%)			
r-MSSD (ms)	108,9±7,4*** (186%)	113,3±6,0 *** (194%)	109,5±7,9*** (172%)	93,3±7,5** (160%)
P	p>0,05		p>0,05	
Control	27,2±4,1 (100%)			
pNN50	42,3±3,2** (155%)	42,2±2,7** (155%)	42,3±3,3** (155%)	35,4±3,0 (129%)
P	p>0,05		p>0,05	
Control	2432,3±24,6 (100%)			
LF	3209,9±328,1* (131%)	3774±228,13*** (155%)	3539,2±299,7*** (145%)	3259,6±303,6** (134%)
P	p>0,05		p>0,05	
Control	1645±120,6 (100%)			
HF	2654,2±253,5*** (161%)	2642,2±229,6 *** (159%)	2640,2±255,3*** (160%)	2348,1±256,7** (142%)
Control	0,021±0,003 (100%)			
HRVTI	0,0258±0,007 (122%)	0,0250±0,005 (119%)	0,018±0,0008 (85%)	0,022±0,003 (104%)
P	p>0,05		p>0,05	
Control	1,209±0,06 (100%)			
LF/HF	1,4±0,11 (116%)	1,3±0,08 (108%)	1,4±0,2 (116%)	1,3±0,2 (108%)
P	p>0,05		p>0,05	
Control	0,8±0,03 (100%)			
Segm, ST, mm depression	1,1±0,1** (137%)	0,9±0,01** (112%)	1,08±0,08** (135%)	1,3±0,08*** (162%)
P	p<0,05		p>0,05	

Note: SDNN *– standard deviation of NN intervals;* ***SDNNi*** *– index – average in 24 hours interval* ***NN*** *standard deviations within 5 minutes of time, r-MSSD – square root of the sum of square differences in NN interval during 24 hours;* ***pNN50*** *– number NN intervals, different from the previous mode after with more than 50 ms, expressed as a percentage of the total number NN intervals; statistically significant differences compared to control group * p <0,05, ** p <0,01, *** p <0,001*

value reductio in dynamics in group II by 18%. LF parameter values presented conclusive changes compared to the control group I initially noting an increase by 31%, while in group II - up to 45% respectively, in dynamics this index rose up to 55% in group I and decreased by 11% in study group II. HRVTI index changes in group I were initially increased up to 22%, for the other group being unchanged compared with the control group, but in dynamics in group I decreased by

3%. LF / HF ratio had an identical increase for both groups compared to the control group, reaching the value of 16% and then decreased by 8% respectively in each group. Average initial ST segment depression constituted an increase up to 37% in group I and 35% in study group II, following a 25% reduction for investigated group I and 27% increase from the initial value in the group II. ST segment depression assessment confirms the degree of hypoxia of the heart with the onset of metabolic disorders in the myocardium. Evolution of heart rate variability parameters in the general group of patients with chronic heart failure secondary to arterial hypertension are noted in Table 4.

The result of the group's dynamic analysis of heart rate variability in patients with HTA (n = 52) after a thorough editing of the main ECG events the time parameters were automatically determined as: SDNN, SDNNi, SDANN, r-MSSD, pNN50 that noted significantly increased values compared with the control group at inclusion in the study phase and the spectral ones that also showed conclusive increases than the control group. Dynamic evaluation of these parameters showed irregular oscillations, values being significantly increased compared with the control group, confirming the result of metabolic disturbances that occured after myocardial hypoxia processes underlying changes in cardiac electrophysiology in chronic myocardial dysfunctions.

DISCUSSIONS

In fundamental researches it was proved that, pathogenetic mechanisms that trigger in the chronic dysfunctions of the myocardium and can be objectified by analyzing the heart rate variability, include neurotoxicity induced by catecholamines, which is supported by non-enzymatic autooxidation of catecholamines to form hinnom. To this end, we determined the mechanism of neurotoxicity of catecholamines, where the process of deamination of catecholamines was firstly studied being represented by two stages: 1- initial intermediate metabolites formation of highly reactivity in the form of aldehydes under the action of monoaminooxidase; 2-transformation of the intermediate reactivity metabolites in the form of highly reactive aldehydes in deaminated inert and stable metabolites (8). In clinical and experimental studies it was found that, in cases of exhaustion of energy sources the intracellular pH is reduced, which is characteristic of ischemia and hypoxia, and also a rapid and significant release of catecholamines being produced in the cytoplasm of neurons, but the degree damage is directly proportional to the increase of the concentration of metabolites, which contributes to processes including deamination of catecholamines in the mechanisms of cell injury (9).

The second cardiac effect of sympathetic hyperactivity is β-adrenergic receptors desensitization, receptors through which catecholamines' modulating myocardial contractility activity is exerted. In carrying β-adrenergic receptors desensitization several mechanisms interfere, and the first of them is the decrease of β1 adrenergic receptors „down regulation" (10).

Normally, at the level of myocardial cell the β1 adrenergic receptors and β2 receptors domi-

TABLE 4. *Evolution of heart rate variability parameters in patients with chronic myocardial dysfunctions secondary to arterial hypertension*

Index	Study group (n = 52) initial	Study group (n = 52) 6 months	p	Control group
FCC med	80.7±1.5	75.7±0.8*	p<0.01	84.5±3.4
SDNN (ms)	216.7±7.5***	197.6±6.7*	p >0.05	168.3±10.2
SDNNi (ms)	113.9±4.0**	121.6±5.4***	p> 0.05	89.1±6.2
SDANN (ms)	194.3±6.2***	176.2±5.8***	p <0.05	108.6±8.5
r-MSSD (ms)	109.3±5.4***	103.5±4.9***	p> 0.05	58.11±8.8
pNN50	43.3±2.3**	38.9±3.0*	p> 0.05	27.2±4.1
LF	3374.5±221.3***	3517.0±210.3***	p> 0.05	2432.3±24.6
HF	3647.2±178.8***	2495.1±171.7***	p <0.001	1645±22.6
HRVTI	0.022±0.003	0.023±0.003	p> 0.05	0.021±0.003
LF/HF	1.44±0.09*	1.3±0.07	p> 0.05	1.209±0.06
Segm. ST, mm depression	1.1±0.06***	1.2±0.07***	p> 0.05	0.8±0.03

Note: SDNN *– standard deviation of NN intervals;* ***SDNNi*** *– index – average in 24 hours interval* ***NN*** *standard deviations within 5 minutes of time, r-MSSD – square root of the sum of square differences in NN interval during 24 hours;* ***pNN50*** *– number NN intervals, different from the previous mode after with more than 50 ms, expressed as a percentage of the total number NN intervals; statistically significant differences compared to control group * p <0.05, ** p <0.01, *** p <0.001*

nate representing only 20-30% of the total number of receptors. In chronic heart failure and in its progression, the number of β1-adrenergic receptors decreases while increasing the relative proportion of β2 receptors, whose stimulation realizes a more reduced contraction than β1-receptors stimulation, reaching to 30-40% of the total adrenergic - β receptors (10).

An important significance is provided to pathogenetic mechanism of chronic myocardial dysfunctions onset represented by RGC system (complex receptor-G-protein adenylyl cyclase), resulting in a decrease in the activation of adenylyl cyclase and adenylmonophosphate formation, resulting in decreased contractile force. The third mechanism relates to the operation of RGC system itself in which the formation of cAMP (cyclic adenosinmonophosphate) is stimulated by Gs protein (stimulatory G protein) and is inhibited by Gi protein (inhibitory G protein) (10).

Thus, in some studies done in heart failure a low level of Gs protein function was detected, but normally in other. Therefore the realized research found 30-40% increase in Gi protein activity leading to decreased contractile force (10).

Thus, all these mechanisms of dysregulation of β-adrenergic receptors result in decreased contractile response to stress and firstly to physical overstrain, reduced response by 50% comparing with the contractile normal response to the exogenous administration of β-agonists. (11,12)

CONCLUSIONS

1. Due to the results of this study we came to the conclusion that, in children and adolescents with arterial hypertension occurred changes in cardiac electrophysiology being defined both by occurrence of heart rhythm disorders such as sinus tachycardia in 63.5%, sinus bradycardia in 3, 8% of cases, changes in QRS morphology in 88.5% of cases, supraventricular extrasystole in 11.5% of cases, ventricular extrasystole in 11.5% of cases, abnormal remodeling processes in the left ventricle in 94.2% of cases, signs of left ventricular myocardial hypertrophy in 61.5% of cases.

2. In the patients examined in this study significant changes in heart rate variability parameters were determined, which suggests a disorder of regulatory systems in cardiac electrophysiology and influences significantly the clinical status of patients and the development of chronic myocardial dysfunctions.

The variability parameters specific changes of heart rate in chronic heart failure secondary to arterial hypertension influences the prognosis of patients with an increased risk of sudden death.

3. It is important to detect early signs of heart failure in this group of patients and initiate pathogenetic treatmen to support the heart's pumping function without increasing the myocardium oxygen demand. This requires choosing the group of preparations, particularly ACEI inhibitors either alone or in combination therapy (ACEI + aldosterone inhibitor) individually selected according to the patient's clinical indications.

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