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обеспечивающих очистку от патогенов. Этот механизм может нарушаться при дисбалансе вегетативных рефлексов и нейропептидов, который развивается у детей с синдромом вертебробазиллярной артериальной системы (СВБАС).

Цель исследования - определение нейрогенного обеспечения патогенеза рекуррентных бронхитов у детей с синдромом вертебробазиллярной артериальной системы путем изучения сывороточного содержания веществ, влияющих на секреторно-эвакуаторную функцию бронхов и активность воспалительного процесса - субстанция Р, вазоактивный интестинальный пептид и эндотелин-1.

Обследовано 90 детей в возрасте от 7 до 11 лет, сформировано 3 группы наблюдения: I группа – дети с РБ и СВБАС

(n=30); II группа – дети с СВБАС без РБ (n=30); III группа – дети с РБ без СВБАС (n=30).

В I группе в сравнении со II и III отмечалось увеличение количества детей с высоким сывороточным содержанием субстанции Р - на 66,7% и 50,0%, соответственно ( $p<0,05$ ) и эндотелина-1 - на 23,3% и 40,0%, соответственно ( $p<0,05$ ), низким содержанием вазоактивного интестинального пептида - на 46,7% и 23,4%, соответственно ( $p<0,05$ ).

Таким образом, следует заключить, что у детей с РБ и СВБАС основой тяжелого течения бронхита является дисбаланс сывороточного уровня провоспалительной субстанции Р, вазоактивного интестинального пептида и эндотелина-1.

## რეზიუმე

P სუბსტანციის, ენდოთელინ-1 და ვაზოაქტიური ინტენსტინალური პეპტიდის შემცველობა რეკურენტული ბრონქიტით და ვერტებრობაზილური უკმარისობით ბავშვების სისხლის შრატში

ტ.სლუცკაია, ლ.ოვჩარენკო, ა.ვერტეგელი, ა.კრიაჟევი, ი. სამოხინი

სახელმწიფო დაწესებულება “უკრაინის ჯანდაცვის სამინისტროს ზაპოროჟიეს დილპომის შემდგომი განათლების სამედიცინო აკადემია”, უკრაინა

რეკურენტული ბრონქიტების (რბ) მიმდინარეობა განპირობებულია ბრონქების სეკრეტორულ-ევაკუატორული მექანიზმებით, რომლებიც უზრუნველყოფს პათოგენებისაგან გაწმენდას. აღნიშნული მექანიზმები შეიძლება დაზიანდეს ვერტებრალური რეფლექსების და ნეიროპეპტიდების დისბალანსის დროს, რომელიც ვითარდება ბავშვებში ვერტებრობაზილური არტერიული სისტემის სინდრომის (ვასს) პირობებში.

კვლევის მიზანს წარმოადგენდა რეკურენტული ბრონქიტების პათოგენეზის ნეიროგენული უზრუნველყოფის შესწავლა ბავშვებში ვერტებრობაზილური არტერიული სისტემის სინდრომით იმ ნივთიერებათა შრატოვანი შემცველობის განსაზღვრით, რომლებიც ზეგავლენას ახდენს ბრონქების სეკრეტორულ-ევაკუატორულ ფუნქციაზე და ანთებითი პროცესის აქტივობაზე - P სუბსტანცია, ენდოთელინ-1 და ვაზოაქტიური ინტენსტინალური პეპტიდი.

დაკვირვება მიმდინარეობდა 7-11 წლის 90 ბავშვზე,

რომლებიც გაყოფილი იყო ჯგუფად: I ჯგუფი – ბავშვები რბ-ით და ვასს-ით (n=30); II ჯგუფი – ბავშვები ვასს-ით რბ-ის გარეშე (n=30); III ჯგუფი – ბავშვები რბ-ით ვასს-ს გარეშე (n=30).

ჩატარებული კვლევის შედეგად დადგენილია, რომ I ჯგუფში შედარებით II და III ჯგუფებთან აღინიშნა ბავშვების რიცხვის მატება მაღალი შრატოვანი შემცველობის P სუბსტანციით - 66,7% და 50%, შესაბამისად ( $p<0,05$ ), ენდოთელინ-1 - 23,2% და 40%, შესაბამისად ( $p<0,05$ ) და ვაზოაქტიური ინტენსტინალური პეპტიდის დაბალი შემცველობით - 46,7% და 23,4%, შესაბამისად ( $p<0,05$ ). ყოველივე ზემოაღნიშნულის გათვალისწინებით ავტორებს გამოტანილი აქვთ დასკვნა, რომ ბავშვებში რბ-ით და ვასს-ით ბრონქიტის მიმდინარეობის მიზეზს წარმოადგენს ანთებისმიერი P სუბსტანციის, ენდოთელინ-1-ის და ვაზოაქტიური ინტენსტინალური პეპტიდის შრატისმიერი დონის დისბალანსი.

## PLASMA microRNA-133a LEVEL IN PATIENTS WITH ESSENTIAL ARTERIAL HYPERTENSION

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Essential arterial hypertension (EAH) is not only one of the most common cardiovascular (CV) diseases, but also a risk factor for a large number of other CV diseases, as well as cerebrovascular diseases and kidney diseases [8,9].

EAH causes damage to a number of vital organs such as a heart, vessels, kidneys, brain and retina [3,8]. The damage of these organs remains asymptomatic for a long time and is defined by the term «asymptomatic hypertension-mediated organ

damage» (HMOD [8]). The main HMOD includes: increased arterial stiffening; left ventricular hypertrophy (LVH); microalbuminuria, or elevated albumin-creatinine ratio; moderate or severe chronic kidney diseases (CKD) and advanced retinopathy [8,30,32]. Over time with not effective enough therapy asymptomatic HMOD transforms into established CV (cerebrovascular disease (ischemic stroke, cerebral hemorrhage, transient ischemic attack (TIA), coronary artery disease (CAD) (myocardial infarction, angina, myocardial revascularization), atheromatous plaque, heart failure, peripheral artery disease, atrial fibrillation) or renal disease [3,8]. It is development of these established CV or renal diseases that determines that EH is the leading cause all-cause mortality, premature death and disability-adjusted life years in Europe [2,25].

The main mechanisms of pathogenesis of EAH include the following: neural mechanisms (resetting of the baroreceptors, increase efferent sympathetic nerve activity to the heart, vasculature and kidney, which increase heart rate, systemic and renal vasoconstriction, vascular and heart hypertrophy, renin release and enhance renal sodium and water reabsorption) [13,27]; renal mechanisms (acquired or inherited defect in the kidneys' ability to excrete the excessive sodium load with resetting of the pressure-natriuresis curve, which prevents the return of blood pressure to normal) [37]; vascular mechanisms (endothelial cell dysfunction with impaired release of endothelium-derived relaxing factors (e.g., nitric oxide) and enhanced release of endothelium-derived constricting, proinflammatory, prothrombotic and growth factors, violation of processes of angiogenesis and arteriogenesis, vascular remodeling) [12,15,21]; metabolic mechanisms (dyslipidaemia, oxidative stress, insulin resistance) [4,31]; hormonal mechanisms (first of all activation of renin-angiotensin-aldosterone system, which plays one of the main roles in the development of endothelial cell dysfunction, vascular and heart remodeling and hypertensive end-organ damage) [15,37]. All the mechanisms described lead to the progression of EH.

In recent years, much attention in the study of the pathogenesis of EAH and its complications has been paid to molecular genetic studies. To date, the results of studying the gene polymorphism of a number of powerful factors that regulate vascular tone, inflammation, hypertrophy and fibrosis of the myocardium and remodeling of the vascular wall have been published [29]. At the same time, in addition to genetic variations associated with the primary changes in DNA molecules, an important reason for the development and progression of a number of CV diseases are epigenetic factors regulating gene expression, which include microRNAs (miRs) [1,39].

MiRs are small, non-coding RNA molecules 18-25 nucleotides in length which bind to the potential target gene site in the 3' untranslated region of specific target messenger RNA (mRNA) and act as posttranscriptional regulators of gene expression [34].

According to current studies, miRs play a significant role in the pathogenesis of EAH [17,22,41]. When studying the pathogenesis of EAH and HMOD, the miRs -133 family and, first of all, miR-133a are of particular interest [20,24]. MiR-133a is specific for muscle tissue, mainly expressed in cardiomyocytes, vascular smooth muscle cells, in skeletal muscle, is important in regulating the growth, differentiation and proliferation of these cells [14,24]. MiR-133a is also involved in the regulation of endothelial function and angiogenesis, apoptosis of endothelial and vascular smooth muscle cells [28]. In recent years, the role of miR-133a in the mechanisms of regression of hypertrophy and myocardial fibrosis has been discussed [10,26].

The aim of research was investigation of the plasma miR-133a level in patients with EAH.

**Material and methods.** 45 patients with EAH, 27 (60%) male and 18 (40%) female, at the average age ( $52,14 \pm 7,25$ ) years were enrolled to the study. Control group consisted of 21 healthy persons comparable of age and sex (12 (57%) male and 9 (43%) female, at the average age ( $44,14 \pm 3,17$ ) years. Examination was carried out in the department of hypertension and kidney disease of Government institution "L.T. Malaya Therapy National Institute of the National Academy of medical science of Ukraine".

Research was performed due to Helsinki Declaration; the protocol was approved by local ethics committee of Government institution "L.T. Malaya Therapy National Institute of the National Academy of medical science of Ukraine" (Protocol №8, 29.08.2016). Informed consent was obtained from each patient.

Among the examined patients, 20 (44%) patients had grade 2 EAH, 25 (56%) - grade 3. Overweight was diagnosed in 24 (53%) patients. Dyslipidemia was diagnosed in 33 (73%) patients. Pre-diabetes (impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT) was diagnosed in 6 (13%) patients. Asymptomatic hyperuricemia (HUE) was detected in 13 (29%) patients.

The following HMODs were diagnosed: increased arterial stiffness - in 12 (27%) patients, LVH - in 25 (55%), the presence of atheromatous plaque on imaging - in 18 (40%) patients, microalbuminuria - in 7 (15%), moderate CKD in - 10 (22%) patients.

Established CV diseases were detected in 16 (24%) patients, of which in 5 (11%) patients were identified stable coronary artery disease (SCAD) (stable angina, Class I (Canadian Cardiovascular Society Classification) and 8 (18%) - chronic heart failure (CHF) NYHA (Class I) with preserved ejection fraction (HFpEF).

The examination did not include patients with secondary hypertension, acute CV diseases, stable angina, above class II (according to the Canadian Cardiovascular Society Classification), CHF with mid-range (HFmrEF) and reduced ejection fraction (HFrEF) and with HFpEF with NYHA Class II and higher, obesity, diabetes mellitus, as well as patients suffering from acute or chronic inflammatory processes, chronic kidney diseases, clinically expressed diseases of the liver, endocrine organs and blood.

Patients underwent generally accepted clinical, laboratory and instrumental testing. The determination of serum lipid levels was carried out by an enzymatic method using the analyzer "Humareazer 2106-1709" (Germany). Blood glucose, creatinine, urea, and uric acid levels were determined by the enzyme method using the analyzer "Humareazer 2000" (Germany).

The morphological and functional parameters of the heart were studied using the standard echocardiographic method in the B and M modes using the «Aloka SSD 280 LS» ultrasound complex (Japan). The mass of the myocardium of the left ventricle (MMLV) and the MMLV index (LVMI) were calculated by the formula of the American Society of Echocardiography [8,23].

The presence of atheromatous plaque was detected by ultrasound of common carotid arteries with color Doppler blood flow mapping using an ultrasound scanner "LOGIQ 5" (CIIA) [8].

The classification of EAH was carried out according to the degree of increase in office blood pressure (BP) (EAH of 1 degree was diagnosed with systolic BP 140–159 mmHg and/or diastolic BP 90–99 mmHg, Grade 2 - with systolic BP 160–179 mmHg and/or diastolic BP 100–109 mmHg) in accordance with the 2018 ESC/ESH recommendations [8].

The following criteria were used to identify the main risk factors. Overweight was diagnosed at body mass index (BMI)  $\geq 25$  kg/m<sup>2</sup> (height<sup>2</sup>) and  $<30$  kg/m<sup>2</sup> (height<sup>2</sup>) [38].

Dyslipidaemia was diagnosed by revealing elevated levels of total cholesterol (TC) ( $\geq 4.5$  mmol/L) or low-density lipoprotein-cholesterol (LDL-C) ( $\geq 2.5$  mmol/L - for high-risk patients and  $\geq 1.8$  mmol/L - for very high-risk patients) [6]. IFG was diagnosed when fasting plasma glucose was 5.6-6.9 mmol/L, IGT - when fasting plasma glucose was  $< 7.0$  mmol/L and 2-h post-load plasma glucose was 7.8-11.0 mmol/L [3].

Asymptomatic HUE was recorded with an increase in blood uric acid levels of more than 360  $\mu\text{mol/L}$  (as recommended by the European League against Rheumatism) [36].

HMODs were diagnosed based on the following criteria: increased arterial stiffness - when pulse pressure was  $> 60$  mmHg [8], LVH (according to echocardiography) - when LVMI was: men  $> 50$   $\text{g/m}^2$ ; women  $> 47$   $\text{g/m}^2$  (height in  $\text{m}^2$ ) (in overweight patients), or LVMI/body surface area (BSA)  $\text{g/m}^2 > 115$  (men) and  $> 95$  (women) (in normal-weight patients) [8]; the presence of atheromatous plaque was identified by the carotid intima media thickness (CIMT)  $> 1.5$  mm, or by a focal increase in thickness of 0.5 mm or 50% of the surrounding carotid IMT value [8]; microalbuminuria - when urine albuminuria was 30-300 mg/24 h [8]; moderate CKD - when eGFR was  $> 30$ -59 mL/min/1.73  $\text{m}^2$  BSA [8,18].

Established CV disease was also diagnosed in accordance with the recommendations of the ESH/ESC: SCAD (stable angina) - in accordance with the 2013 ESC guidelines for the management of stable coronary artery disease [5], HFpEF - in accordance with the 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure [7].

MiR was isolated from 300  $\mu\text{L}$  of plasma using "NucleoSpin miRNA Plasma" kit (Macherey-Nagel, Germany). The miR concentration was determined using "Qubit 3" (Life Technologies, USA) using the "Qubit<sup>TM</sup> microRNA" (Thermo Fisher Scientific) reagent kit. Reverse transcription was performed using the "TaqMan MicroRNA Reverse Transcription Kit" (Applied Biosystems, USA) and a specific loop primer Hsa-miR-133a (assay ID 002246, Applied Biosystems, USA). Analysis of the miR level was performed by real-time polymerase chain reaction (PCR) using the «CFX96 Touch» (BioRad) detection system and the reagent kits for monitoring and analyzing miR expression «TaqMan microRNA Assay» and «TaqMan<sup>®</sup> Universal PCR Master Mix» (Thermo Fisher Scientific, USA) in accordance with the manufacturers instructions. Small nuclear RNA U6 (U6 snRNA assay ID 001973, Applied Biosystems, USA) was used as an endogenous control for reverse transcription and amplification. Analysis and calculation of the relative normalized miR level was performed using CFX Manager Software (BioRad).

For the statistical processing of the results SPSS 21 software for Windows XP was used. Statistical analyzes of the data were performed using descriptive statistics, the Mann-Whitney U-test, the Wilcoxon W-test, the  $\chi^2$  test, and correlation analysis. The main research data are presented in the form of a median and interquartile range (Me [25%; 75%]) due to the fact that the distribution of signs proposed for analysis and study differed from the normal law of distribution. Check for normality was carried out according to the criterion of Shapiro-Wilk. Differences were considered statistically significant at  $p < 0.05$ .

**Results and their discussion.** When studying the levels of miR-133a in the blood plasma of patients with EAH and in the control group, the following results were obtained. It was established that in patients with EAH level of miR-133a was significantly lower than in practically healthy individuals in the control group (0,182 [0,102; 0,301]) vs (0,382 [0,198; 0,474]),  $p < 0.05$ ) (Fig. 1).

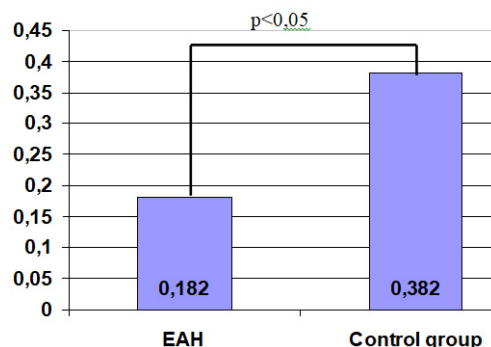


Fig. 1. Levels of miR-133a in blood plasma in patients with EAH and healthy individuals in the control group

In practically healthy individuals and EAH patients, the levels of miR-133a in plasma did not significantly differ depending on gender and age ( $p > 0.05$ ). When analyzing the levels of in plasma miR-133a in patients with EAH depending on the degree of increase in BP (according to office BP levels), no significant differences were found ( $p > 0.05$ ). There were also no statistically significant differences ( $p > 0.05$ ) in the levels of miR-133a in plasma in the subgroups of patients with EAH with or without the following risk factors: a) with overweight and without overweight, b) with and without dyslipidemia, c) with IFG, and/or IGT and normal carbohydrate metabolism, d) with GUE and with normal levels of uric acid in the blood.

In addition, there was no statistically significant difference ( $p > 0.05$ ) in the level of miR-133a in plasma in the examined patients with or without HMOD such as increased arterial stiffness, carotid atheromatous plaque, microalbuminuria and moderate CKD, as well as established CV disease: SCAD and HFpEF.

At the same time, the analysis of miR-133a levels in plasma in patients with EAH, depending on the presence or absence of LVH, showed the following. It was revealed that in patients with EAH who developed HMOD such as LVH, the level of miR-133a in plasma (0,133 [0,099; 0,184]) was significantly lower than in patients without LVH (0,238 [0,155; 0,410]),  $p < 0.05$ ) and also significantly lower than in healthy subjects in the control group (0,382 [0,198; 0,474]),  $p < 0.05$ ). Whereas in contrast to patients with EAH and LVH, the level of miR-133a in plasma of patients with EAH without LVH was not significantly different from those in the control group ( $p > 0.05$ ) (Fig. 2).

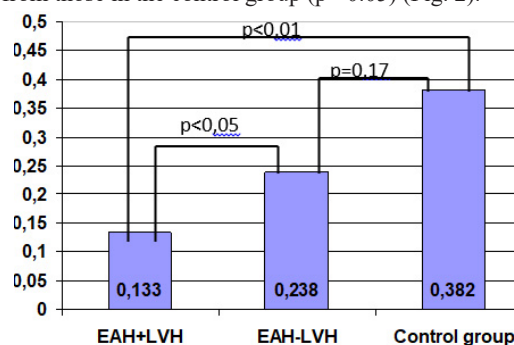


Fig. 2. Levels of miR-133a in plasma in patients with EAH depending on the presence or absence of LVH

For more detailed analysis of the relationship between plasma levels of miR-133a and the clinical, hemodynamic, metabolic and morpho-functional parameters studied in this work, a correlation analysis was performed in patients with EAH. As a result of the

*Table. Correlation between the level of miR-133a in plasma and clinical, hemodynamic, metabolic and morpho-functional parameters in patients with EAH*

| Options                                     | R     | p    |
|---------------------------------------------|-------|------|
| Age, years                                  | 0,09  | 0,41 |
| Weight, kg                                  | 0,06  | 0,61 |
| BMI, kg/m <sup>2</sup>                      | -0,07 | 0,55 |
| Systolic BP, mmHg                           | -0,21 | 0,09 |
| Diastolic BP, mmHg                          | -0,07 | 0,57 |
| Pulse pressure, mmHg                        | -0,16 | 0,20 |
| Heart rate, beats in 1 minute               | 0,09  | 0,42 |
| TC, mmol/L                                  | 0,08  | 0,51 |
| TG, mmol/L                                  | -0,19 | 0,12 |
| LDL-C, mmol/L                               | 0,15  | 0,23 |
| HDL-C, mmol/L                               | -0,02 | 0,91 |
| Fasting plasma glucose, mmol /L             | 0,17  | 0,19 |
| Left atrial volume index, mL/m <sup>2</sup> | 0,01  | 0,98 |
| LV diastolic diameter, mm                   | +0,27 | 0,03 |
| Interventricular septum thickness, mm       | -0,27 | 0,04 |
| LV posterior wall thickness, mm             | -0,28 | 0,03 |
| MMLV, g                                     | -0,17 | 0,18 |
| LVMI g/m <sup>2</sup>                       | -0,32 | 0,01 |
| E/A                                         | 0,26  | 0,08 |

*R - the correlation coefficient between the level of miR-133a in plasma and clinical, hemodynamic, metabolic and morpho-functional parameters in patients with EAH; p - statistical significance of the correlation coefficient*

analysis, a number of reliable pair correlations was revealed (Table). The most significant were the following: the plasma level of miR-133a directly correlated with the LV diastolic diameter ( $R=+0,27$ ;  $p=0,03$ ) and inversely correlated with the interventricular septum thickness ( $R=-0,27$ ;  $p=0,04$ ), the LV posterior wall thickness ( $R=-0,28$ ;  $p=0,03$ ) and the LVMI ( $R=-0,32$ ;  $p=0,01$ ).

Thus, as a result of our studies, we have found a significant decrease in the level of miR-133a in the blood plasma of EAH patients in comparison with practically healthy individuals in the control group.

The results obtained are generally consistent with published single data on the change in the level of circulating miR-133a in the EAH.

So, in Zhang X. et al. [42] in patients with EAH, a decrease in the level of miR-133a in serum was found in comparison with the control group of practically healthy individuals. This work also revealed a decrease in levels in serum and other miRs (199-3p, 21-5p, 1-3p, 208a-3p, 423-5p, 223-3p, 122-5p) against the background of an increase in levels in serum levels of miRs such as 18b-5p, 20b-5h, 548c-3p and 499a-5p. The authors carried out a mathematical analysis of the significance of the studied miRs in the EAH revealed the greatest diagnostic significance of the combination of the following miRs: 199a-3p, 208a-3p, 122-5p and 223-3p. That is, the level of miR-133a in the serum, although it was reduced in these patients with EAH, was not included in the group of the most informative miRs in terms of diagnosing EAH. However, it should be noted that this study was conducted in the Chinese population, which may differ significantly in terms of expression miRs from the European.

Studies of the nature of changes in the level of circulating miR-133a in patients with EAH from the European population

include the work of Kontaraki J.E. et al. [20]. In this work, a significant decrease in the level of expression of circulating miR-133a in mononuclear blood cells in patients with EAH was shown in comparison with that in practically healthy individuals.

In a number of other studies, the level was studied in the EAH of circulating miR-133 as a whole as a family. So, in an earlier work by Kontaraki J.E. et al. [19] found a significant decrease in the expression level of miR-133 in blood cells in patients with EAH in comparison with healthy individuals. However, if in our study no correlation was found between the level of miR-133a and the levels of systolic BP, diastolic BP and pulse pressure, then in the work of Kontaraki J.E. et al. [19] shown significant positive correlations of the expression level of miR-133 with 24-hour ambulatory BP, mean diastolic BP and mean pulse pressure. The simultaneous detection of a decrease in the expression level of miR-133 in patients with EAH and positive correlations of the expression level of this miR with levels of BP that are elevated in the EAH is a clear contradiction and requires further, more in-depth assessments. In a study of Chinese scientists Huang Y-q. et al. [16] a decrease in the expression level of miR-133 in blood cells was also detected, but still at the earliest stage of EAH formation- in patients with white-coat hypertension compared also to practically healthy controls.

Another important result of our study was the discovery of the fact that in patients with EAH with advanced LVH, the level of miR-133a in plasma was significantly lower than in patients with EAH without LVH. Moreover, in our work, it was found that the level of miR-133a in the blood plasma in patients with EAH correlated significantly with a number of echocardiographic parameters: with LV diastolic diameter (direct correlation)

and with indicators of the interventricular septum thickness, the LV posterior wall thickness and the LVMI (inverse correlations).

The differences in the level in plasma miR-133a in EAH patients, depending on the presence or absence of LVH, found in our study also found isolated confirmations in the literature. So, in the work mentioned above, Kontaraki J.E. et al. [20], conducted, as mentioned above among patients of the European population, along with significant decrease in the expression of miR-133a in mononuclear blood cells in patients with EAH compared with healthy individuals, the significant inverse correlation was found between the level of this miR and LVMI ( $R = -0.431$ ,  $P < 0.001$ ). At the same time, in the work mentioned above, Zhang X. et al. [42] serum miR-33a levels in EAH patients were not associated with the presence or absence of LVH and did not correlate with LVMI. It is possible that the lack of relationship between the level of miR-133a and LVH in this study was also due to the fact that the patients did not belong to the European population, but to the Chinese.

The data obtained in our work on reliable changes in the miR-133a levels in the blood of patients with EAH and the connection of these changes with the presence of LVH are quite weighty evidence in experimental studies.

In the recent years, in studies conducted both in vivo and in vitro, a number of effects of the miR-133 as a family and including miR-133a have been identified, which are very important in the regulation of physiological and pathological processes in the CV system.

In particular, it has been shown that miR-133 plays a significant role in the regulation of endothelial function and angiogenesis [33], in vascular smooth muscle cells differentiation, their interaction with endothelial cells [11,35], as well as in apoptosis of endothelial cells and vascular smooth muscle cells [40]. However, the most important function of miR-133a and in general of the miR-133 family is its participation in the development, differentiation of the cardiomyocytes and regulation of the processes of hypertrophy and fibrosis of the myocardium [14,28]. In this regard, the family of miR-133 refers to the so-called «myo-miRs» [10].

According to modern data, the miR-133 family, including miR-133a, is considered as powerful factors that inhibit myocardial hypertrophy and fibrosis, including in response to mechanical overload, in particular pressure overload [26,40]. At the same time, in an experiment on salt-sensitive rats, it was found that high-salt intake in these rats not only leads to an increase in BP, but also to suppression of miR-133a myocardial expression, that initiates fibrosis of animals' myocardium [14].

Thus, the decrease in miR-133a level in plasma in patients with EAH, especially with LVH, revealed by us indicates the important role of the deficiency of this miR in the pathogenesis of both EAH itself and LVH. In this regard, it is promising to find ways to correct the reduced level of miR-133a in order to inhibit the development and progression of EAH and LVH in these patients.

# Conclusions.

1. A significant decrease in plasma levels of miR-133a in patients with EAH compared with healthy individuals has been established.

2. The lowest level of miR-133a in plasma has been detected in patients with the presence of such HMOD as LVH.

3. The findings suggest that the decrease in plasma miR-133a level in patients with EAH plays a significant role both in the pathogenesis of this disease itself and in the mechanisms of development of pathological remodeling of the heart.

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# REFERENCES

1. Berezin A.E., Kremzer A.A. The potential diagnostic and prognostic role of micro-RNAs as biological markers for the onset and progression of heart failure. *Heart and vessels*. 2014; 3: 93-101.
2. Chow C.K., Teo K.K., Rangarajan S., Islam S., Gupta R., Avezum A., Bahonar A., Chifamba J., Dagenais G., Diaz R., Kazmi K., Lanas F., Wei L., Lopez-Jaramillo P., Fanghong L., Ismail N.H., Puoane T., Rosengren A., Szuba A., Temizhan A., Wielgosz A., Yusuf R., Yusufali A., McKee M., Liu L., Mony P., Yusuf S. PURE Study Investigators. Prevalence, awareness, treatment, and control of hypertension in rural and urban communities in high-, middle-, and low-income countries. *JAMA*. 2013; 310:959–968.
3. 2013 ESH/ESC Guidelines for the management of arterial hypertension. *Journal of Hypertension* 2013, 31:1281–1357.
4. ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD: the Task Force on diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and developed in collaboration with the European Association for the Study of Diabetes (EASD). *Eur Heart J*. 2013 Oct;34 (39):3035-87.
5. 2013 ESC guidelines on the management of stable coronary artery disease. *Eur Heart J*. 2013; 34, 2949–3003.
6. 2016 ESC/EAS Guidelines for the Management of Dyslipidaemias. *Eur Heart J*. 2016; 37, 2999–3058.
7. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J*. 2016; 37, 2129–2200.
8. 2018 ESC/ESH Guidelines for the management of arterial hypertension. *Eur Heart J*. 2018; 39, 3021–3104.
9. Forouzanfar MH, Liu P, Roth GA, Ng M, Biryukov S, Marczak L, Alexander L, Estep K, Hassen Abate K, Akinyemiju TF, Ali R, Alvis-Guzman N, Azzopardi P, Banerjee A, Barnighausen T, Basu A, Bekele T, Bennett DA, Biadgilign S, Catala-Lopez F, Feigin VL, Fernandes JC, Fischer F, Gebru AA, Gona P, Gupta R, Hankey GJ, Jonas JB, Judd SE, Khang YH, Khosravi A, Kim YJ, Kimokoti RW, Kokubo Y, Kolte D, Lopez A, Lotufo PA, Malekzadeh R, Melaku YA, Mensah GA, Misganaw A, Mokdad AH, Moran AE, Nawaz H, Neal B, Ngalesoni FN, Ohkubo T, Pourmalek F, Rafay A, Rai RK, Rojas-Rueda D, Sampson UK, Santos IS, Sawhney M, Schutte AE, Sepanlou SG, Shifa GT, Shiue I, Tedla BA, Thrift AG, Tonelli M, Truelsen T, Tsilimparis N, Ukwaja KN, Uthman OA, Vasankari T, Venketasubramanian N, Vlassov VV, Vos T, Westerman R, Yan LL, Yano Y, Yonemoto N, Zaki ME, Murray CJ. Global burden of hypertension and systolic blood pressure of at least 110 to 115mmHg, 1990-2015. *JAMA*. 2017;317: 165–182.
10. Gangwar R.S., Rajagopalan S., Natarajan R., Deiluiis J.A. Noncoding RNAs in Cardiovascular Disease: Pathological Relevance and Emerging Role as Biomarkers and Therapeutics. *American Journal of Hypertension*, 2018; 31 (2): 150–165.
11. Gao S, Wassler M, Zhang L, Li Y, Wang J, Zhang Y, Shelat H, Williams J, Geng Y-J. MicroRNA-133a regulates insulin-like growth factor-1 receptor expression and vascular smooth muscle cell proliferation in murine atherosclerosis. *Atherosclerosis*. 2014; 232:171–179.

12. Ghiadoni L., Virdas A., Taddei S. Endothelial damage: measurement and clinical importance. In: Manual of hypertension of the European Society of Hypertension / editor by G. Mancia, G. Grassi, J. Redon. 2014; 211-221.
13. Grassi G., Brambilla G., Dell'Oro R., Seravalle G. Impaired autonomic cardiovascular control in hypertension. In: Manual of hypertension of the European Society of Hypertension / editor by G. Mancia, G. Grassi, J. Redon. 2014; 135-139.
14. Guo T-S., Zhang J., Mu J-J., Liu F-Q., Yuan Z-Y., Ren K-Y., Wang D. High-Salt Intake Suppressed MicroRNA-133a Expression in Dahl SS Rat Myocardium. *Int. J. Mol. Sci.* 2014; 15(6): 10794-10805.
15. Hall M.E., Hall J.E. Pathogenesis of hypertension. In: Hypertension: a companion to Braunwald's heart disease/editor by Bakris G.L., Sorrentino M.J. 2018: 33-51.
16. Huang Y-q., Huang C., Chen J-y., Li J., Feng Y-q. The association of circulating miR-30a, miR-29 and miR-133 with white-coat hypertension. *Biomark Med.* 2016; 10(12):1231-1239.
17. Jalnapurkar S., Mangaonkar A., Mondal A., Burke J., Fulzele S., Kolhe R. MicroRNAs: as a Novel Potential Tool for Diagnosis, Prognosis, and Therapeutic Agents in Hypertension// *Journal of Hypertension and Cardiology.* 2015; 1 (4): 14-22.
18. KGIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease Kidney International. Supplements. Volume 3.Issue 1. January 2013; doi:10.1038/kisup.2012.48.
19. Kontaraki J.E., Marketou M.E., Zacharis E.A., Parthenakis F.I., Vardas P.E. Differential expression of vascular smooth muscle-modulating microRNAs in human peripheral blood mononuclear cells: novel targets in essential hypertension. *J Hum Hypertens.* 2014; 28:510-516.
20. Kontaraki J.E., Marketou M.E., Parthenakis F.I., Maragkou-dakis S., Zacharis E.A., Petousis S., Kochiadakis G.E., Vardas P.E. Hypertrophic and antihypertrophic microRNA levels in peripheral blood mononuclear cells and their relationship to left ventricular hypertrophy in patients with essential hypertension. *JASH*; 2015, 9 (10): 802-810.
21. Koval S., Mysnychenko O., Snigurska I., Penkova M., Vysotskaya E., Bozhko V., Strashnenko A. Blood levels of angiopoietin-2 proangiogenic and proinflammatory factor in patients with essential hypertension. *Journal of Hypertension.* 2015; Vol. 33, e Supplement 1: 25th European Meeting on Hypertension and Cardiovascular Protection, Milan, 12-15 June 2015: Abstracts. PP. 23.11, e 340.
22. Koval S., Yushko K., Snihurska I., Starchenko T., Miloslavsky D., Penkova M. Role of microRNA in the development of arterial hypertension. *Arterial hypertension.* 2017; 5(55):17-21.
23. Lang R.M., Bierig M., Devereux B. et al. Recommendation for chamber quantification. *Eur. J. of Echocardiogr.* 2006; Vol. 7, 79-108.
24. Leimena C., Qiu H. Non-Coding RNA in the Pathogenesis, Progression and Treatment of Hypertension. *Int. J. Mol. Sci.* 2018; 19, 927.
25. Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet.* 2002; 360:1903-1913.
26. Li N., Zhou H., Tang Q. miR 133: A Suppressor of Cardiac Remodeling? *Frontiers in Pharmacology.* 2018; 9: 903.
27. Martin E.A., Victor G.R. Premise, promise, and potential limitations of invasive devices to treat hypertension. *Curr Cardiol Rep.* 2011; 13:86-92.
28. Navickas R., Diane G. D., Laucevicius A., Taparauskaitė A., Zdanyte M., Holvoet P. Identifying circulating microRNAs as biomarkers of cardiovascular disease: a systematic review. *Cardiovascular Research.* 2016; 111:322-337.
29. Padmanabhan S., Caulfield M., Dominiczak A. Genetic basis of blood pressure and hypertension. In: Manual of hypertension of the European Society of Hypertension / editor by G. Mancia, G. Grassi, J. Redon. 2014; 115-127.
30. Perrone-Filardi P., Coca A., Galderisi M., Paolillo S., Alpendurada F., de Simone G., Donal E., Kahan T., Mancia G., Redon J., Schmieder R., Williams B., Agabiti-Rosei E. Noninvasive cardiovascular imaging for evaluating subclinical target organ damage in hypertensive patients: a consensus article from the European Association of Cardiovascular Imaging, the European Society of Cardiology Council on Hypertension and the European Society of Hypertension. *J Hypertens* 2017; 35:1727-1741.
31. Redon J., Martinez F., Fabia M.J. The metabolic syndrome in hypertension. In: Manual of hypertension of the European Society of Hypertension/ edited by G. Mancia, G. Grassi and J. Redon. CRC Press. 2014; 433-442.
32. Sehestedt T., Jeppesen J., Hansen T.W., Wachtell K., Ibsen H., Torp-Pedersen C., Hildebrandt P., Olsen M.H. Risk prediction is improved by adding markers of subclinical organ damage to SCORE. *Eur Heart J.* 2010; 31:883-891.
33. Soufi-Zomorrod M., Hajifathali A., Kouhkan F., Mehdizadeh M., Sman R., Soleimani M. MicroRNAs modulating angiogenesis: miR-129-1 and miR-133 act as angio-miR in HUVECs. *Tumour Biol J Int Soc Oncodevelopmental Biol Med.* 2016; doi: 10.1007/s13277-016-4845-0.
34. Sun Li-Li S., Wen-Dong L., Feng-Rui L., Xiao-Qiang L. The regulatory role of microRNAs in angiogenesis-related diseases. *J Cell Mol Med.* 2018; 22:4568-4587.
35. Torella D., Iaconetti C., Catalucci D., Ellison G.M., Leone A., Waring C.D., Bochicchio A., Vicinanza C., Aquila I., Curcio A., Condorelli G., Indolfi C. MicroRNA-133 controls vascular smooth muscle cell phenotypic switch in vitro and vascular remodeling in vivo. *Circ Res.* 2011; 109:880-893.
36. 2016 updated EULAR evidence-based recommendations for the management of gout. *Ann Rheum Dis.* 2017; 76:29-42. doi:10.1136/annrheumdis-2016-209707 Published Online First 9 November 2016.
37. Victor R.G., Libby P. Systemic hypertension: Management. In: Braunwald's heart disease: a textbook of cardiovascular medicine /edited by D.L. Mann, D.P. Zipes, P. Libby, R.O. Bonow, E. Braunwald-10 edition/. 2015; 953-979.
38. WHO: Obesity: Prevention and managing the global epidemic. Technical Report Series 894. Geneva: WHO; 2000.
39. Wojciechowska A., Braniewska A., Kozar-Kamińska K. MicroRNA in cardiovascular biology and disease. *Adv Clin Exp Med.* 2017; 26 (5):865-874.
40. Xin M., Olson E.N., Bassel-Duby R. Mending broken hearts: cardiac development as a basis for adult heart regeneration and repair. *Nat Rev Mol Cell Biol.* 2013; 14:529-541.
41. Zhang Z., Joyce B.T., Kresovich J.K., Zheng Y., Zhong J., Patel R., Zhang W., Dou C., McCracken J.P., DöÄaz A., Motta V., Sanchez-Guerra M., Bian S., Bertazzi P.A., Schwartz J., Baccarelli A.A., Wang S., Hou L. Blood pressure and expression of microRNAs in whole blood. *PLoS ONE.* 2017; 12(3): e0173550.
42. Zhang X., Wang X., Wu J., Peng J., Deng X., Shen Y., Yang C., Yuan J., Zou Y. The diagnostic values of circulating miRNAs for hypertension and bioinformatics analysis. *Biosci Rep.* 2018; 38(4).

## SUMMARY

### PLASMA microRNA-133a LEVEL IN PATIENTS WITH ESSENTIAL ARTERIAL HYPERTENSION

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The aim of research was to investigate the plasma microRNA (miR-133a) level in patients with essential arterial hypertension (EAH).

A total of 45 patients with EAH 2-3 degrees aged  $52.14 \pm 8.25$  years and 21 healthy individuals (control group) with comparable age and sex distributions.

The following frequency of risk factors was revealed among the examined patients: overweight (53%), dyslipidaemia (73%), pre-diabetes (13%), asymptomatic hyperuricemia (29%); hypertension-mediated organ damage: increased arterial stiffness (27%), left ventricular hypertrophy (55%), atherosclerotic plaque in the carotid artery (40%), microalbuminuria (15%), moderate stage of chronic kidney disease (22%) and cardiovascular diseases: stable ischemic heart disease (11%) and heart failure with preserved ejection fraction of NYHA functional class I (18%).

The plasma miR-133a level was determined by polymerase chain reaction using “CFX96 Touch” detection system (BioRad) and “TaqMan microRNA Assay” and “TaqMan® Uni-

versal PCR Master Mix” reagents (Thermo Fisher Scientific, USA).

It has been established that in patients with EAH the plasma level of miR-133a was significantly lower than in practically healthy individuals (0,182 [0,102; 0,301]), vs (0,382 [0,198; 0,474]),  $p < 0.05$ ). It has also been revealed a significant decrease in the level of miR-133a in the blood plasma in patients with such organs damage as LVH (0,133 [0,099; 0,184]) in comparison with patients without LVH (0,238 [0,155; 0,410]),  $p < 0.05$ ) and also significantly lower than in healthy subjects in the control group (0,382 [0,198; 0,474]),  $p < 0.05$ ). There were no statistically significant differences in the plasma levels of miR-133a in the group of patients with EAH, depending on the presence of risk factors, other organ damage and cardiovascular diseases.

The findings suggest the significant role of reducing of plasma levels of miR-133a in the pathogenesis of hypertension itself and in pathological remodeling of the heart.

**Keywords:** essential arterial hypertension, microRNA-133a, left ventricular hypertrophy.

## РЕЗЮМЕ

### УРОВЕНЬ микроРНК- 133а В ПЛАЗМЕ КРОВИ БОЛЬНЫХ ЭССЕНЦИАЛЬНОЙ АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИЕЙ

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Целью исследования явилось изучение уровня микроРНК-133а в плазме крови больных эссенциальной артериальной гипертензией.

Обследованы больные эссенциальной артериальной гипертензией (ЭАГ) II-III степени в возрасте  $52,14 \pm 7,25$  лет ( $n=45$ ) и практически здоровые лица ( $n=21$ ) - контрольная группа, сопоставимая по полу и возрасту. Среди обследованных больных выявлены следующие факторы риска: избыточная масса тела - 52%, дислипидемия - 73%, преддиабет - 13%, асимптоматическая гиперурикемия - 29%; поражения органов, обусловленные гипертензией: повышенная артериальная жесткость - 27%, гипертрофия левого желудочка (ГЛЖ) - 55%, атеросклеротическая бляшка в сонной артерии - 40%, микроальбуминурия - 15%, умеренная стадия хронической болезни почек - 22% и сердечно-сосудистые заболевания - стабильная ишемическая болезнь сердца - 11% и сердечная недостаточность с сохраненной фракцией выброса I функционального класса по NYHA - 18%.

Уровень микроРНК-133а в плазме крови определяли ме-

тодом полимеразной цепной реакции с помощью системы детекции “CFX96 Touch” (BioRad) и наборов реагентов “TaqMan microRNA Assay” и “TaqMan® Universal PCR Master Mix” (Thermo Fisher Scientific, США).

Установлено, что у больных ЭАГ уровень микроРНК-133а достоверно ниже, чем у практически здоровых лиц - 0,182 [0,102; 0,301] против 0,382 [0,198; 0,474] ( $p < 0.05$ ). Обнаружено также достоверное снижение уровня микроРНК-133а в плазме крови у больных с таким поражением органов, как ГЛЖ (0,133 [0,099; 0,184]) в сравнении с больными без ГЛЖ (0,238 [0,155; 0,410]),  $p < 0.05$ ) и практически здоровыми лицами контрольной группы (0,382 [0,198; 0,474]),  $p < 0.05$ ). Статистически значимых различий в уровнях микроРНК-133а в группе больных ЭАГ в зависимости от наличия изученных факторов риска, кроме ГЛЖ, не выявлено.

Полученные данные свидетельствуют о значимой роли снижения уровня микроРНК-133а в плазме крови у больных ЭАГ, как в патогенезе самой гипертензии, так и патологического ремоделирования сердца.

