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The risk factors of cardiovascular disorders in children with chronic bronchopulmonary diseases

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The purpose was to determine the features of cardiovascular system morphofunctional state and the risk factors for cardiovascular disorders formation in children with chronic bronchopulmonary diseases.

Materials and methods. We examined 144 patients aged 3–16 years (mean age was 11.3 ± 1.2 years) with chronic bronchopulmonary pathology (60 patients with cystic fibrosis with pancreatic insufficiency and 84 patients with heavily treated or partially treated persistent bronchial asthma) and 68 conditionally healthy children who made up the control group. A complex of functional methods for cardiovascular system studying in patients with chronic bronchopulmonary diseases included: echodopplercardiography with determination of left ventricular myocardium geometry, Holter monitoring of cardiac activity, duplex scanning of the common carotid artery by intima-media thickness measuring of the common carotid artery wall and examining the index of endothelial stress shift. To determine the risk factors for cardiovascular disorders development in children with chronic bronchopulmonary diseases, a method E. N. Shigan was used to normalize intensive indicators, based on the Bayesian probabilistic method. A prognostic model of cardiovascular disorders development was obtained using the exponential regression equation for patients with chronic bronchopulmonary diseases.

Results. According to results of the study it has been found that there is a structural and functional restructuring of the left ventricular myocardium on the background of the cardiac activity vegetative regulation violation and vascular remodeling in children with chronic bronchopulmonary diseases. The definition of risk factors for cardiovascular complications development in children with bronchial asthma has showed the followings: the presence of chronic infection (OR = 8.4), the age of child from 3 to 6 years (OR = 4.9), the disease duration more than 3 years (OR = 2.3), the circadian index value less than 1,2 units (OR = 3.1) and QTc interval prolongation more than 420 ms (OR = 2.1). The main risk factors for cardiovascular disorders formation in the group of children with cystic fibrosis were the age of the child from 3 to 6 years (OR = 4.0), contamination of the respiratory tract by *Pseudomonas aeruginosa* (OR = 4.0), severe course of the disease (OR = 3.3), the presence of chronic infection (OR = 6.0), the body mass index less than P_{50} (OR = 4.2) and the QTc interval duration more than 420 ms (OR = 1.4). The risk of cardiovascular complications was increased with the presence of 3 or more risk factors that confirmed by the equation of exponential regression in the group of patients with chronic bronchopulmonary diseases.

Conclusions. The development of cardiovascular complications is caused by a combination of many factors in children with chronic bronchopulmonary diseases. It is necessary to include into the algorithm for examination heart echodopplerography, Holter heart rate monitoring, duplex scanning of the common carotid artery with determination of the endothelial stress index shift and intima-media thickness at least twice a year for the purpose of cardiovascular disorders early diagnosis in children with chronic bronchopulmonary diseases, having 3 or more risk factors for cardiovascular complications. Timely detection of a risk group for cardiovascular disorders development will allow the full implementation of preventive measures and medications for cardiovascular disorders correcting in children with chronic bronchopulmonary diseases.

Key words: pulmonary disease, cystic fibrosis, asthma, child, cardiovascular system.

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Фактори ризику формування кардіоваскулярних розладів у дітей із хронічними захворюваннями бронхолегеневої системи

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Мета роботи – визначити особливості морфофункціонального стану серцево-судинної системи та фактори ризику формування кардіоваскулярних розладів у дітей із хронічними захворюваннями бронхолегеневої системи.

Матеріали та методи. Обстежили 144 хворих віком 3–16 років (середній вік – 11,3 ± 1,2 року) з хронічною бронхолегеневою патологією (60 хворих на муковісцидоз з панкреатичною недостатністю та 84 хворих на важку контрольовану або частково контрольовану персистуючу бронхіальну астму), а також 68 умовно здорових дітей, які ввійшли в контрольну групу. Комплекс функціональних методів дослідження серцево-судинної системи у хворих на хронічні бронхолегеневі захворювання включав еходоплеркардіографію з визначенням геометрії міокарда лівого шлуночка, Холтерівський моніторинг серцевої діяльності, дуплексне сканування загальної сонної артерії з вимірюванням товщини комплексу інтима-медія стінки загальної сонної артерії та дослідженням показника напруження зсуву ендотелію. Для визначення факторів ризику розвитку серцево-судинних порушень у дітей, які хворі на хронічні захворювання бронхолегеневої системи, застосовували метод нормування інтенсивних показників Е. Н. Шигана, що ґрунтується на імовірнісному методі Байеса. Прогностична модель розвитку серцево-судинних розладів для хворих на хронічні захворювання бронхолегеневої системи отримана за допомогою рівняння експоненційної регресії.

Результати. Встановили, що в дітей із хронічними бронхолегеневими захворюваннями відбувається структурно-функціональна перебудова міокарда лівого шлуночка на тлі порушення вегетативної регуляції серцевої діяльності та ремоделювання судин. Визначення факторів ризику розвитку серцево-судинних ускладнень у дітей, які хворі на бронхіальну астму, показало: найбільшу інформативність мали наявність хронічних вогнищ інфекції (ВШ = 8,4), вік дитини від 3 до 6 років (ВШ = 4,9), тривалість захворювання понад 3 років (ВШ = 2,3), значення циркадного індексу менше ніж 1,2 одиниці (ВШ = 3,1) та подовження інтервалу QTc понад 420 мс (ВШ = 2,1). Основні фактори ризику формування серцево-су-

Ключові слова: легеневі захворювання, муковісцидоз, астма, діти, серцево-судинна система.

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динних розладів у групі дітей, які хворі на муковісцидоз: вік дитини від 3 до 6 років (ВШ = 4,0), обсіменіння дихальних шляхів *Pseudomonas aeruginosae* (ВШ = 4,0), тяжкий перебіг захворювання (ВШ = 3,3), наявність хронічних вогнищ інфекції (ВШ = 6,0), індекс маси тіла менше ніж P_{50} (ВШ = 4,2) та тривалість інтервалу QTc понад 420 мс (ВШ = 1,4). Ризик виникнення серцево-судинних ускладнень у групі хворих на хронічні бронхолегеневі захворювання зростав за наявності 3 і більше факторів ризику, що підтверджено рівнянням експоненційної регресії.

Висновки. Розвиток кардіоваскулярних ускладнень у дітей із хронічними захворюваннями бронхолегеневої системи зумовлений поєднанням багатьох чинників. Для ранньої діагностики серцево-судинних порушень у дітей, які хворі на хронічні бронхолегеневі захворювання і мають 3 і більше чинників ризику виникнення кардіоваскулярних ускладнень, в алгоритм обстеження доцільно включати еходоплерографію серця, Холтерівський моніторинг серцевого ритму, дуплексне сканування загальної сонної артерії з визначенням показника напруження зсуву ендотелію та товщини комплексу інтима-медіа не рідше, ніж двічі на рік. Своєчасне виявлення групи ризику з розвитку серцево-судинних розладів у дітей, які хворі на хронічні захворювання бронхолегеневої системи, дасть змогу в повному обсязі реалізувати профілактичні заходи та медикаментозні способи корекції кардіоваскулярних порушень.

Ключевые слова: легочные заболевания, муковисцидоз, астма, дети, сердечно-сосудистая система.

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Факторы риска формирования кардиоваскулярных нарушений у детей с хроническими заболеваниями бронхолегочной системы

Е. Е. Пашкова, Г. А. Леженко

Цель работы – определить особенности морфофункционального состояния сердечно-сосудистой системы и факторы риска формирования кардиоваскулярных расстройств у детей с хроническими заболеваниями бронхолегочной системы.

Материалы и методы. Обследовали 144 больных в возрасте 3–16 лет (средний возраст – 11,3 ± 1,2 года) с хронической бронхолегочной патологией (60 больных муковисцидозом с панкреатической недостаточностью и 84 больных тяжелой контролируемой или частично контролируемой персистирующей бронхиальной астмой), а также 68 условно здоровых детей, составивших контрольную группу. Комплекс функциональных методов исследования сердечно-сосудистой системы у больных хроническими бронхолегочными заболеваниями включал эходопплеркардиографию с определением геометрии миокарда левого желудочка, Холтеровское мониторирование сердечной деятельности, дуплексное сканирование общей сонной артерии с измерением толщины комплекса интима-медиа стенки общей сонной артерии и исследованием показателя напряжения сдвига эндотелия. Для определения факторов риска развития сердечно-сосудистых нарушений у детей с хроническими заболеваниями бронхолегочной системы применяли метод нормирования интенсивных показателей Е. Н. Шигана, основанный на вероятностном методе Байеса. Прогностическая модель развития сердечно-сосудистых расстройств у детей с хроническими заболеваниями бронхолегочной системы получена с помощью уравнения экспоненциальной регрессии.

Результаты. Установлено, что у детей с хроническими бронхолегочными заболеваниями происходит структурно-функциональная перестройка миокарда левого желудочка на фоне нарушения вегетативной регуляции сердечной деятельности и ремоделирования сосудов. Определение факторов риска развития сердечно-сосудистых осложнений у детей, больных бронхиальной астмой, показало: наибольшую информативность имели наличие хронических очагов инфекции (ОШ = 8,4), возраст ребенка от 3 до 6 лет (ОШ = 4,9), длительность заболевания более 3 лет (ОШ = 2,3), значение циркадного индекса менее 1,2 единиц (ОШ = 3,1) и удлинение интервала QTc более 420 мс (ОШ = 2,1). Основные факторы риска формирования сердечно-сосудистых расстройств в группе детей, больных муковисцидозом: возраст ребенка от 3 до 6 лет (ОШ = 4,0), обсеменение дыхательных путей *Pseudomonas aeruginosae* (ОШ = 4,0), тяжелое течение заболевания (ОШ = 3,3), наличие хронических очагов инфекции (ОШ = 6,0), индекс массы тела менее P_{50} (ОШ = 4,2) и удлинение интервала QTc более 420 мс (ОШ = 1,4). Риск возникновения сердечно-сосудистых осложнений у детей с хроническими заболеваниями возрастал при наличии 3 и более факторов риска, что подтверждалось уравнением экспоненциальной регрессии.

Выводы. Развитие кардиоваскулярных осложнений у детей с хроническими заболеваниями бронхолегочной системы обусловлены сочетанием многих факторов. Для ранней диагностики сердечно-сосудистых нарушений у детей с хроническими бронхолегочными заболеваниями, имеющих 3 и более факторов риска возникновения кардиоваскулярных осложнений, в алгоритм обследования целесообразно включать эходопплерографию сердца, Холтеровское мониторирование сердечного ритма, дуплексное сканирование общей сонной артерии с определением показателя напряжения сдвига эндотелия и толщины комплекса интима-медиа не реже, чем 2 раза в год. Своевременное выявление группы риска по развитию сердечно-сосудистых расстройств у детей с хроническими заболеваниями бронхолегочной системы позволит в полном объеме реализовать профилактические мероприятия и медикаментозные способы коррекции кардиоваскулярных нарушений.

The respiratory diseases rate is among the highest in the structure of children and adolescents morbidity, among which a significant proportion belongs to chronic bronchopulmonary diseases [1]. Annually, the number of children with chronic respiratory diseases increases by 5–6 % [2]. Taking into account that one of the chronic respiratory diseases complications, which not only determine the disease clinical course severity, but also can determine the disease outcome, are cardiovascular disorders [3,4]. The lung diseases should be considered as inextricably linked to the cardiovascular system state [5]. Cardiovascular disorders in bronchopulmonary disease are potentially reversible in childhood, which requires a proper assessment of their development risk for a certain patient and timely correction [6]. Questions concerning the risk of disease development stratification are directly related to the prognosis of pathological process course as well as assessment of potential therapy and drugs rational choice [7].

The purpose

The purpose of this study was to determine the features of cardiovascular system morphofunctional state and the risk factors for cardiovascular disorders development in children with chronic bronchopulmonary diseases.

Materials and methods

144 patients aged 3–16 years (mean age was 11.3 ± 1.2 years) with chronic bronchopulmonary disease were examined. The first group consisted of 60 patients with cystic fibrosis with pancreatic insufficiency, the second – 84 patients with heavily treated or partially treated bronchial asthma. Patients received baseline therapy in accordance with the clinical protocols for children with bronchial asthma and cystic fibrosis [8,9]. The control group consisted of 68 healthy children, representative of age and sex.

The complex of functional methods for cardiovascular system examination of patients with chronic bronchopulmonary diseases included: Doppler echocardiography, Holter monitoring of cardiac activity and duplex scan of the common carotid artery. The ultrasound examination of the heart was performed using the Medison SonoAce 8000 ultrasound machine (USA) according to the standard procedure. Morphometric indicators were normalized to the surface area of the body. To study the processes of the left ventricular remodeling left ventricular mass index (LVMI) as a ratio LVM (left ventricular mass) / height in meters^{2,7} was calculated and the remodeling parameter was the left ventricle wall relative thickness. Left ventricular geometry was classified as normal, concentric remodeling, concentric hypertrophy and eccentric hypertrophy [10].

For the diagnosis of the LV diastolic dysfunction preclinical stage, the Functional Compliance Index (FCI) was determined using A. N. Rosenbaum and V. T. Koval (2010) method [11]. For this purpose, the normalized coefficient (NC) was calculated as the ratio of the stroke volume (SV) to the LVM in the control group, which, regardless of age, was 0.8 cu. After this, the correlation coefficient (CC) between the SV and LVM in the groups of patients was calculated and the functional conformity index value, expressed as the ratio CC / IV, was determined for the left ventricle myocardium state. The FCI was considered as normal if its values were from 0.8 to 1.2 cu. When the value of FCI exceeded 1.2 cu the early stage of left ventricle dysfunction, accompanied by a hyperkinetic type of hemodynamics, was established; if the FCI value was less than 0.8 cu, left ventricle diastolic dysfunction was diagnosed.

A duplex scan of the common carotid artery was performed by sensor with a frequency of 5–10 MHz on the Medisson 8000 (USA) device. The carotid wall intima-media thickness (IMT) measurement was carried out using the standard procedure P. Pignollii (1986): in the common carotid artery on 1.0–1.5 cm proximal to bifurcation in the maximal section on the posterior wall of the artery in the diastole (relative to the sensor), the IMT measurement from the inner wall of intima to the outer wall of media excluding the size of the adventitia [12]. We have formed groups representing the patient's age considering the carotid artery diameter and the IMT size depending on age. The average age of patients with bronchial asthma was 12.4 ± 1.0 years, patients with cystic fibrosis – 12.3 ± 1.2 years. The average age of the control group children was within 12.2 ± 1.3 years. To study the effect of blood flow on a vessel wall the shear stress on endothelium (τ) was investigated, which was calculated by the formula [13]:

$$\tau = 4\eta V / D \quad (1)$$

η: the blood viscosity (average 0.05 Ps);

V: the maximum blood flow velocity in the common carotid artery;

D: diameter of the artery (cm).

The Holter monitoring of cardiac rhythm was carried out at the hardware and computer complex "CardioSens" (STC KhAI "Medica"). The detected dynamic series of cardiointervals were processed using a mathematical analysis of heart rate variability (HRV). The HRV was evaluated in temporal and spectral analyzes in accordance with the International Standards for Measurement, Physiological Interpretation and Clinical Use, developed by the Working Group of the European Cardiology Society and the North American Society for Cardiac Stimulation and Electrophysiology [14].

The mathematical analysis and statistical processing of data were performed on a PC using the licensed software package of Statistic for Windows 6.1.RU using variational, correlation, regression and nonparametric methods of statistical analysis. To develop a mathematical model for predicting the risk of cardiovascular disorders development the method of intensive indicators normalization E. N. Shigan (1986) was used in children with chronic bronchopulmonary diseases based on the Bayesian probabilistic method [15]. The prognostic model of cardiovascular disorders development was obtained using the equation of exponential regression for patients with chronic bronchopulmonary diseases.

Results and discussion

According to our studies, a structural and functional reorganization of the right heart with the secondary pulmonary hypertension development occurred in children with chronic pathology of the bronchopulmonary system. At the same time, signs of pulmonary hypertension had 35.7 % of patients with bronchial asthma and 58.2 % of children with cystic fibrosis. The study of the left ventricular myocardium morphofunctional state in children with chronic bronchopulmonary pathology revealed the presence of the left ventricular myocardium remodeling due to the increase in LVM and the left ventricle walls thickening in 49 % of patients with bronchial asthma and in 58 % of patients with cystic fibrosis. Among the variants of left ventricle remodeling concentric (20 %) and eccentric (21 %) hypertrophy predominated in children with bronchial asthma. Concentric remodeling was found in 8 % of patients. Among the variants of left ventricular myocardial remodeling in the vast majority of patients from group with cystic fibrosis eccentric hypertrophy was determined – 24 %. Morphometric parameters of the left ventricular myocardium in 19 % of patients corresponded to the criteria for concentric remodeling, and in 15 % of patients, concentric left ventricular hypertrophy was observed.

The calculation of FCI, as an indicator of the left ventricle diastolic dysfunction preclinical stage, has showed that in children with chronic bronchopulmonary diseases, there was a significant decrease in this indicator relative to

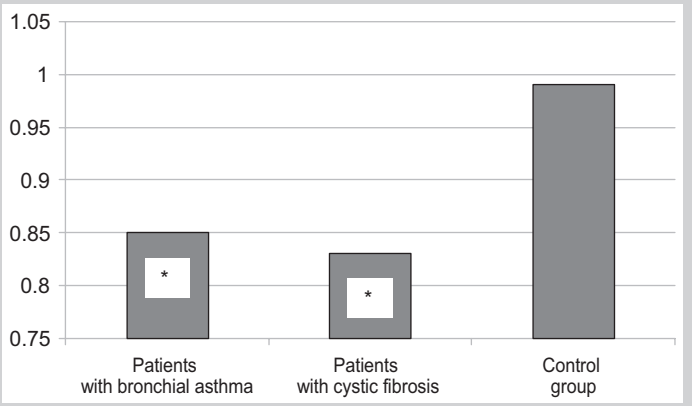

Fig. 1. The FCI value of observation groups.

*: P < 0.05 – in comparison with the control group values.

Table 1. The indicators of circadian index, average daily values of QT and QTc intervals for Holter monitoring of ECG in children with chronic bronchopulmonary pathology (M ± m)

Indicators, units	Patients with bronchial asthma n = 84	Patients with cystic fibrosis n = 60	The control group n = 68
Heart rate, bpm.	87.5 ± 1.3	94.1 ± 1.9*	84.8 ± 1.1
Circadian Index, cu	1.28 ± 0.01	1.26 ± 0,01*	1.31 ± 0.01
QT, mc	344.3 ± 2.7	333.0 ± 3.7*	348.5 ± 2.6
QTc , mc	412.9 ± 1.8	413.0 ± 2.0	412.6 ± 1.8
QTc 320–420 mc, %	64.5 ± 3.1*	57.4 ± 4.7*	83.4 ± 2.2
QTc> 420 mc, %	34.8 ± 3.1*	53.6 ± 4.8*	15.7 ± 2.2

*: P < 0.0 5 – in comparison with the control group values.

Table 2. The intima-media complex thickness (IMT) and the shear stress index of the common carotid artery of children with chronic bronchopulmonary diseases (M ± m)

Indicators	Patients with bronchial asthma, n = 20	Patients with cystic fibrosis, n = 20	The control group, n = 20
IMT, mm	0.66 ± 0.02	0.78 ± 0.03*	0.70 ± 0.02
τ, dyn / cm^2	28.94 ± 1.93*	21.24 ± 2.66*	36.04 ± 2.27

*: P < 0.05 – in comparison with the control group values.

the control group, and the mean values were 0,85 ± 0,02 cu in the group of patients with bronchial asthma and 0,83 ± 0,02 cu in the children group with cystic fibrosis versus 0.99 ± 0.02 cu of the control group, P < 0.05 (*Fig. 1*).

The use of the FCI allowed diagnosing signs of left ventricle diastolic dysfunction already at the preclinical stage in 35.9 % of children with bronchial asthma and 37.5 % of children with cystic fibrosis. On the background of left ventricle diastolic dysfunction development the left ventricular myocardium geometry was changed, mainly by the type of concentric remodeling and concentric hypertrophy in all observation groups.

We have carried out the analysis of HRV, which is considered as the most optimal method for the body regulatory systems functioning disorders identifying, taking into account the fact that violations in the organism regulatory systems state precede the hemodynamic disorders appearance. According to the results of study it has been found that changes in the cardiac rhythm variability neural regulation were observed as the attenuation of parasympathetic nervous system tonic influences, increased sympathetic regulation of the autonomic nervous system, and suppression of autonomic circuit activity of cardiac rhythm regulation in children with chronic bronchopulmonary disease. Excessive activity of the sympathetic nervous system led to a number of pathological effects development, including myocardium electrical instability, which was manifested by increased heart rate, decreased circadian index and lengthened corrected QT-interval in children with chronic bronchopulmonary diseases (*Table 1*).

The obtained data testified to depletion of heart rhythm regulation adaptive reserves and formation of heart rhythm rigidity. Owing to the revealed changes, the development of systolic left ventricular myocardium dysfunction occurred, leading to the left ventricular myocardial hypertrophy formation in patients. In turn, left ventricular myocardial remodeling caused an increase in the stress degree of the cardiovascular system mechanisms of regulation in children with chronic bronchopulmonary diseases. In patients with normal left ventricular myocardial mass the state of adaptive-compensatory regulatory systems was characterized by optimal or moderate functional stress.

But with the development of left ventricle myocardial hypertrophy, significant functional tension and vegetative regulatory systems homeostasis imbalance with simultaneous disturbance of heart rhythm various contours of regulation were observed.

The next stage of our work was the study the hemodynamic and tonic-elastic properties of the common carotid artery in children with chronic and relapsing bronchopulmonary diseases.

The data obtained indicated a decrease in the endothelial shear stress index in patients with bronchial asthma at 28.94 ± 1.93 dyn / cm^2 in relation to the control group 36.04 ± 2.27 dyn / cm^2 (P < 0.05), results are presented in *Table 2*.

The lowest values of the endothelial shear stress index were recorded in patients with left ventricular diastolic dysfunction signs (the correlation coefficient between the exponent τ and FCI was r = +0.41, P < 0.05). In the group of patients with cystic fibrosis there were also signs of vascular remodeling, as evidenced by the significantly higher thicknesses of IMT that were 0.78 ± 0.03 mm relative to 0.70 ± 0.02 mm in the control group (p < 0,05) along with a 41% decrease in the endothelial shear stress index (21.24 ± 2.66 dyn/cm^2, P < 0.05).

The IMT value was 0.66 ± 0.02 mm in the group of patients with bronchial asthma, and had no statistical difference from the control group values (P > 0.05). The maximum values of IMT were recorded in patients with cystic fibrosis with severe course of the disease (r = -0.33, P < 0.05) and left ventricular myocardial hypertrophy (r = +0.54, P < 0.05). The changes in the intima-media thickness were determined with the left ventricle diastolic dysfunction development in patients with cystic fibrosis. When performing the correlation analysis, an inverse relationship was established between the IMT thickness of the FCI (r = -0.59, P < 0.05). We recorded the highest pressure in the pulmonary artery in this group of children (r = +0.53, P < 0.05).

Thus, the left ventricular myocardium structural and functional restructuring was observed against the back-

ground of cardiac activity vegetative regulation violation and vascular remodeling in children with chronic bronchopulmonary diseases. According to the study results, risk factors for cardiovascular disorders formation were identified in children with chronic bronchopulmonary diseases. The risk of cardiovascular disorders in chronic bronchopulmonary pathology should be assessed depending on child's sex and age, disease duration and severity, frequency of relapses, chronic infection presence, physical development state (by body mass index), adjusted QT-interval duration and circadian index.

The determination of cardiovascular complications development risk factors for children with bronchial asthma has showed that most informative were the followings: the presence of chronic infection (OR = 8.4, 95 % CI 2.7–25.7; RR = 3.4, 95 % CI 1.6–7.0; P < 0.05), age of the child from 3 to 6 years (OR = 4.9, 95 % CI 2.0–11.7; RR = 1.9, 95 % CI 1.4–2.5; P < 0.05), the disease duration more than 3 years (OR = 2.3, 95 % CI 1.1–4.7; RR = 1.5, 95 % CI 1.1–2.0, P < 0.05). The risk of cardiovascular disorders increased with circadian index values of less than 1.2 in patients with bronchial asthma (OR = 3.1, 95 % CI 1.0–10.9; RR = 1.6, 95 % CI 1.0–2.5, P < 0.05) and QTc interval prolongation with monitoring more than 420 ms (OR = 2.1, CI 1.0–5.5; RR = 1.4, 95 % CI 1.6–7.0; P < 0.05).

According to the study results, the main risk factors for cardiovascular disorders in the group of children with cystic fibrosis were the followings: age of the child from 3 to 6 years (OR = 4.0, 95 % CI 1.5–10,6; RR = 1,6, 95 % CI 1.2–2.0; P < 0.05), the airway contamination by Pseudomonas aeruginosa (OR = 4.0, 95 % CI 1.9–8.7; RR = 1.7, 95 % CI 1.3–2.2; P < 0.05), the disease severe course (OR = 3.3, 95 % CI 1.5–7.0; RR = 1.6, CI 1.2–2.0, P < 0.05), the chronic infection presence (OR = 6.0, 95 % CI 2.1–17.6; RR = 2.1, 95 % CI 1.3–3.6; P < 0.05), the body mass index less than P_{50} (OR = 4.2, 95 % CI 2.0–4.7; RR = 1.8, 95 % CI 1.3–2.4, P < 0.05) and QTc interval prolongation with monitoring more than 420 ms (OR = 1.4, 95 % CI 0.5–3.7; RR = 1.3, 95 % CI 0.5–3.4, P < 0/05).

The risk of cardiovascular complications has been increasing depending on the risk factors number in the group of patients with chronic diseases. In the presence of 1–2 risk factors in one group, the odds ratio was not statistically significant, but if there were 3 or more risk factors for cardiovascular disorders occurrence, it increased 12–26 times. At the same time, the risk of cardiovascular disorders was in the presence of 3 or more risk factors in the group of children with bronchial asthma: OR = 5.2 (95 % CI 2.6–10.8, P < 0.05), RR = 2.2 (95 % CI 1.1–4.6; P < 0.05) and in the group of patients with cystic fibrosis: OR = 19.0 (95 % CI 8.0–48.8, P < 0.05) , RR = 1.9 (95 % CI 1.2–3.0; P < 0.05).

The prognostic model for cardiovascular disorders development was made on the basis of the exponential regression equation, depending on the risk factors number for patients with chronic bronchopulmonary diseases, which was as follows:

$$Y = 0.818e^{0,5294x}, \quad (2)$$

Y: is the probability of syndrome development;

X: is the number of risk factors.

If there is a Y value of more than 1.5 units, there is a risk of cardiovascular disorders development (*Fig. 2*).

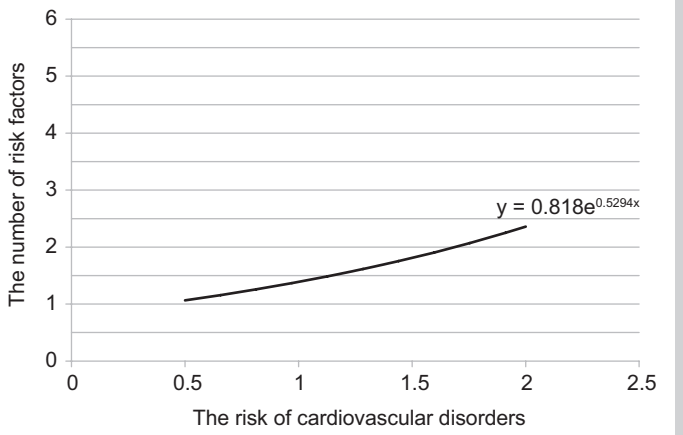

Fig. 2. The risk of cardiovascular disorders depending on the risk factors presence in children with chronic bronchopulmonary diseases.

Thus, a structural and functional restructuring of the left ventricular myocardium is observed against a background of cardiac activity vegetative regulation violation and vascular remodeling in children with chronic bronchopulmonary diseases. It is believed that left ventricle myocardial hypertrophy is one of adaptive mechanisms, which allows the myocardium to cope with increased stress in conditions of pulmonary hypertension.

At the same time, left ventricle myocardial hypertrophy causes a high risk of cardiovascular complications, which is associated with a violation of coronary hemodynamics, heart systolic and diastolic dysfunction development and chronic heart failure [17]. A characteristic feature of morphofunctional changes in the left ventricular myocardium was the diastolic dysfunction development, as an early criterion which can be used as an FCI indicator in children with recurrent and chronic bronchopulmonary diseases. Using FCI made it possible to diagnose the signs of left ventricular diastolic dysfunction already at the preclinical stage in children with recurrent and chronic bronchopulmonary diseases. The results obtained by us are confirmed by the works of M. E. Abdalla and H. A. E. Azeem (2013), which showed that patients formed left ventricle diastolic dysfunction even in the absence of right ventricle diastolic dysfunction with bronchopulmonary system pathology [18]. The revealed disorders were accompanied by the sympathetic nervous system activation that could be considered as a compensatory mechanism aimed at cardiac output supporting in children with chronic bronchopulmonary pathology [19]. An unfavorable consequence of this activation is increased left ventricular tension and increased myocardial oxygen demand, which leads to cardiomyocyte hypertrophy, increased left ventricular volume and changes of left ventricular myocardial function [20].

The morphofunctional changes in the left ventricle myocardium occurred against a background of elastic properties disturbance and vessels remodeling in children with chronic bronchopulmonary diseases. This was confirmed by a decrease in the endothelial stress index shift and an increase in the IMT thickness at the common carotid artery level. One of the reasons for left ventricle myocardium and vessels structural and functional changes is the develop-

ment of endothelial dysfunction [21]. Another factor that plays the main trigger role of ventricular myocardium and vascular remodeling and diastolic dysfunction formation is systemic chronic inflammation [22]. This statement is confirmed by our previous studies [23,24] and is consistent with the work of other researchers [25–27]. Timely diagnosis of cardiovascular disorders, when changes are not pathological but adaptive, and effect on the main components of pathogenesis will allow for cardiovascular changes regression and long-term cardiovascular consequences prevention in children with chronic bronchopulmonary diseases [28].

The determination of cardiovascular disorders predictors and the use of a prognostic model for their development will allow us to identify a risk group for cardiovascular complications development and timely initiate therapeutic measures for their prevention and treatment in children with chronic bronchopulmonary pathology.

Conclusions

1. The development of cardiovascular complications is caused by a combination of many factors in children with chronic bronchopulmonary diseases. The main risk factors for cardiovascular disorders occurrence in children with bronchial asthma are the followings: the presence of chronic infection, the child age 3–6 years, the disease duration more than 3–5 years, the circadian index less than 1.2 cu. In children with cystic fibrosis the child age 3–6 years old, the airway contamination by Pseudomonas aeruginosa, the severe course of disease, the presence of protein-energy deficiency and chronic infection are the most informative risk factors.

2. With the purpose of cardiovascular disorders early diagnosis if there are 3 and more risk factors, it is necessary to include heart echodopplerography, Holter's heart rate monitoring, complete carotid duplex scanning with determination of endothelial shear stress and IMT at least 2 times a year in children with chronic bronchopulmonary diseases.

3. Timely detection of a risk group for cardiovascular disorders development will allow the full implementation of preventive measures and medications for cardiovascular disorders correcting in children with chronic bronchopulmonary diseases.

The prospects. We will form a tactic of therapy for cardiovascular disorders in children with chronic bronchopulmonary diseases based on the findings of the further scientific research.

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