**The state of the cardiovascular system in children with gastroenterological pathological disorders**

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**Summary**: the article deals with the main approaches to the stratification of cardiovascular risk condition of children with gastroenterological disorders; the unmodified risk factors identified by the "Genetic Questionnaire" have been discussed; the role of polymorphism of the folate cycle genes in the development of children’s cardiovascular disease has been identified.

**Key words:** cardiovascular risk, pediatric, cardiovascular system, gastroenterological diseases.

In the recent decades, there has been observed the rapid development of preventive medicine based on measures taken to avoid occurrence of diseases or to diagnose and treat existent diseases in early stages. The numerous risk factors for cardiovascular disease (CVD) development are classified into modified and unmodified [1]. The modified risk factors include the following factors as smoking, dyslipidemia (increased LDL, triglycerides, reduced HDL), high blood pressure, diabetes, obesity, dietary factors, low level of physical activity, alcohol abuse. The CVD unmodified risk factors are personal anamnesis, family anamnesis[2].

The generally recognized criteria by which the severity of CVD prevalence risk is determined are the new lipid and nonlipid factors.

The new lipid risk factors consist of: elevated level of triglycerides, remnants of lipoproteins, small particles of LPN, subtypes of HDL, apolipoproteins B and A-I, ratio of LDL cholesterol / HDL cholesterol [3].

The new nonlipid risk factors include: level of serum homocysteine; thrombogenic/ antithrombogenic factors (platelets and clotting factors, fibrinogen, activated factor VII, plasminogen activation inhibitor-1(PAI-1), tissue plasminogen activator(tPA), von Willebrand factor (vWF), factor V Leiden, protein C, antithrombin III); inflammatory factors; increased levels of fasting glucose [4].

Gene’s polymorphism of folate cycle influences the development of cardiovascular diseases. The aforementioned process can be caused by breach of DNA synthesis that leads to dysregulation of proliferative processes and apoptosis [5]. The causes of the breach of folate cycle include: genetic defects of enzymes (MTHFR, MTR, MTRR), folic acid deficiency, deficiency of vitamins B6 and B12. The course of CVD is more complicated by a combination of several, even moderately expressed aforementioned risk factors compared with the one severely important risk factor.

 Additional risk factors of the disturbance folate cycle include: stomach and intestine disease with malabsorption of vitamins B (ulcerative colitis, Crohn's disease, celiac disease, enteritis, gastritis, peptic ulcer disease); malignant neoplasms of the pancreas and intestine; kidney disease; chronic infection with a long course; prolonged use of anticonvulsants, methotrexate, metformin, H2-receptor antagonists, eufillin, folic acid antagonists, drugs that violate the absorption of folate; factors related to lifestyle (smoking, excessive alcohol consumption, coffee consumption (more than 5 cups of coffee a day); psycho-emotional stress; hypodynamy[6, 7].

The defects of the folate cycle enzymes are accompanied by various microangiopathy locations: "red" hands and feet, cutis marmorata; varix dilatation. The complications associated with homocysteinuria include: mental retardation, mental disorders, convulsions, skeletal disorders, osteoporosis, dislocation of the lens, myopia, iridodonesis. The CNS lesions caused by brainthrombosis are manifested with determined spastic paralysis, paresis, mental deficiency and features of neuro-psychic activity (poor attention switching, low performance capability).Nevertheless classifying patients’ data is one of the major challenges in the stratification process, thorough clinical examination of the patient plays a fundamental part in the diagnosis, risk stratification  and implication of appropriate clinical strategies designed on the received data.

**The aim** of the article is to examine stratification of the risk factors for cardiovascular diseases in children with diseases of the digestive system. The survey was conducted in gastroenterological department of Regional Children's Clinical Hospital in Kharkov in the period from 2015 to 2016, the survey is grounded on the results obtained from the patients’ responses of the "Genetic questionnaire."

**Materials and methods.** The survey respondents were 66 children aged from 2 to 17 years, girls - 32 (48.5%) and boys - 34 (51.5%) with chronic digestive diseases (chronic gastroduodenitis, duodenal ulcer, functional disorders of the biliary tract, pancreatopathy). The average age of the patients was 11, 3± 4, 1 years, primary children of pubertal age (53.0%). The analyzed anthropometric data; generally recognized clinical laboratory and instrumental (ECG, echocardiography) diagnostics, as well as the patient’s responses of the "Genetic questionnaire" were used to verify the children’s diagnoses.

**Results.** The anthropometric data analysis of the exanimated group of children showed that 42.4% of patients had normal level of BMI, 30,2% ±of patients had the increased level of BMI and 24,0% ± of patients had low level of BMI. Thus, among the respondents of surveyed group there were children prone to obesity as well as patients with low body weight. It can be explained by one of the symptoms of gastroenterological diseases, namely, the decreased appetite.

There observed the largest specific gravity in the structure of gastroenterological diseases: 42.4% chronic gastroduodenitis, biliary dyskinesis 15.2%, 12.1% pancreatopathy and duodenal ulcer 9.1%. The aforementioned data are approximately the same as the leading expert’s ones of the current situation in the structure of the pediatric gastroenterological diseases in Ukraine.

At the time of hospitalization all children were conducted objective examination of the cardiovascular system (Table. 1,2,3).

**Table 1**

**Data of the objective research of the cardiovascular system in patients with gastrointestinal diseases.**

|  |  |
| --- | --- |
| Parameters | Value |
| Average SBP, mmHg.( М±σ) | 108,4 ± 11,05 |
| Average DBP, mmHg. (М±σ) | 70,1 ± 7,8 |
| Average heart rate, beats / min (М±σ) | 82,2 ± 11,0 |
| Muffled heart sounds, % | 15 (22,7%) |
| Functional systolic murmur, % | 25 (37,8%) |

Thus, the analysis showed that normal blood pressure had 46 (69.7%) children prehypertension had 7 (10.6%) children, and the stage 1 hypertension had 9 (13.6%) children. The average systolic blood pressure was 108,4 ± 11,05, diastolic blood pressure was 70,1 ± 7,8. Muffled heart sounds was observed in 15 (22.7%) patients, functional systolic murmur in 25 (37.8%).

The following Table 2 displays the features of ECG in the studied patients.

**Table 2**

**Changes of ECG parameters in patients (% the number of patients)**

|  |  |
| --- | --- |
| Character of change of ECG parameters | Number of patients ( in %) |
| Lengthening the interval PQ | 57,6 |
| Lengthening the interval QRS | 18,2 |
| Lengthening the interval QT | 24,2 |
| Changing the interval ST and T wave | 42,4 |
|  Monotop heart rhythm disturbances: | 50,0 |
| * sinus arrhythmia
 | 21,2 |
| * sinus tachyarrhythmia
 | 10,6 |
| * sinus bradyarrhythmia
 | 18,2 |

Thus, only 31.8% of patients had the ECG parameters that correspond to the age norms. Lengthening the interval PQ, T wave changes and the interval ST, QT interval prolongation were frequently registered, consequently, prevailed ECG changes in the examined patients testify disturbances repolarization of myocardium.

According to the electrocardiogram data received in the process of studying the function of automatism, 50% of patients had monotop heart rhythm disturbances; sinus arrhythmia was in 21.21% of patients.

**Table 3**

**The frequency of small structural cardiac abnormalities in pediatric patients**

|  |  |
| --- | --- |
| Anatomical and physiological parameters | Number of patients( in %) |
| Mitral valve prolapse | 24,5% |
| Abnormal chords of the left ventricle | 28,8% |
| Hypertrophy of the papillary muscles and increased trabeculae apparatus of the left ventricle  | 12,1% |

According to the data of ECG, no organic heart disease in any of the patients was registered which was confirmed by echocardiography. Small structural cardiac abnormalities consist of: 28.8% of abnormal trabeculae of the left ventricle and 24.5% (mainly 1 class.) of mitral valve prolapse.

ECHOCG revealed mild dilatation of the left ventricle in 30.3% (in patients with ulcerative colitis, Crohn's disease, celiac disease), other echocardiographic parameters were normal.

 The history of patients was studied in details to identify risk factors for CVS diseases.

According to anamnesis data based on the results of the "Genetic questionnaire", 37.9% of the patients’ parents abused more than five cups of coffee per day, 41.0% of parents are smoking. 22.7% of parents were overweighed, 11.4% suffered from the first level of obesity, 3.8% of parents had the second level of obesity. Type II diabetes had 8.2% of parents and 18.2% others relatives. Furthermore, 36.4% of the surveyed children led a sedentary lifestyle.

**Table 4**

**The results obtained through the use of "genetically questionnaire."**

|  |  |  |  |
| --- | --- | --- | --- |
| Feature | Children | Parents | Siblings |
| Blond hair | 54,5% | 68,5% | 53,0% |
| Blue eyes | 28,8 | 30,3% | 53,0% |
| Pale skin | 19,7% | 24,2% | 15,6% |
| Vascular pattern on the skin | 13,6% | 10,6% | 15,6% |
| Changes in the visual system | 13,6% | 20,0% | 18,8% |
| Diseases of the organ of hearing | 1,5% | 1,5% | 13,6% |
| Diseases of the cardiovascular system | 7,6% | 28,0% | 3,2% |
| Posture abnormalities | 45,5% | 6,9% | 10,6% |
| Propensity to fracture of bones | 15,2% | 3,1% | 1,5% |

Thus, the survey has identified in the children with gastroenterological pathology and their parents the following levels of risk: 41.1% of children (7.6% of the respondents were diagnosed with cardiovascular disease) had family anamnesis with early cardiovascular diseases, 41.0% of smoking parents, 30.2% of children and 37.9% of parents were overweighed or obese.

The examined patients with gastroenterological pathology suffered from changes in the cardiovascular system: 10.6% of children had prehypertension, 13.6% - first stage hypertension, 22.7% - muffled heart sounds, 37.8% - functional systolic murmur. According to the ECG data, deviations were found in 68.2% of the surveyed children; in the process of studying the function of automatism, it was revealed that 50% of patients had monotop heart rhythm disturbances

According to ECG data confirmed by ECHOCG, the symptoms of organic heart disease were not discovered in any of the patients. The small structural cardiac abnormalities include: 28.8% of abnormal chordae of the left ventricle and 24.5% of mitral valve prolapse. Moderate dilatation of the left ventricle was found in 30.3% of children.

The results obtained by the “Genetic questionnaire” revealed phenotypic changes specifying the genetic defects of the folate cycle enzymes, such as blonde hair in 54.5% of children, blue eyes - 28.8%, pale skin - 19.7%, vascular pattern on the skin - 13.6%, changes in the visual system - 13.6%, diseases of the organ of hearing - 1.5%, posture abnormalities - 45.5%, propensity to fracture of bones - 15.2% of the surveyed children. These changes can indicate the presence of microangiopathies of various localization with hyperhomocysteinemia.

However, the possible heterogeneity of these diseases provide basis for implication of the results of genetic studies in the selection and individualization therapy and stratification cardiovascular risk.

**Conclusions:** The clarification the state of the cardiovascular system in children with gastroenterological disorders grounded on the responses of the "Genetic questionnaire" can stratify risk factors for the development of cardiovascular diseases.

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**ABBREVIATIONS AND DESIGNATIONS:**

ANS - autonomic nervous activity

DBP - diastolic blood pressure

ECG – electrocardiography

ECHOCG –echocardiography

CVS - cardiovascular system

GIT - gastrointestinal tract

LV - left ventricle

CG - chronic gastroduodenitis

PUD - Peptic ulcer disease

DU - duodenal ulcer

BW - biliary ways

GERD - gastroesophageal reflux disease