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PEDIATRICS

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THE STATE OF THE CARDIOVASCULAR SYSTEM IN CHILDREN WITH GASTROINTESTINAL DISORDERS

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Summary. The articledeals with themainapproachestostratificationof cardiovascular riskinchildrenwithgastrointestinal disorders.The study focuses onunmodifiedriskfactorsidentifiedby "Geneticquestionnaire".Folatecycle genepolymorphismwas shown to promote thedevelopmentofcardiovasculardiseasesinchildren.

Keywords: cardiovascular risk, children, cardiovascular system, gastrointestinal diseases.

INTRODUCTION

A rapid increase in development of preventive medicine based on measures taken to avoid occurrence of diseases or to diagnose and treat existent diseases at early stages has been observed recently. Numerous risk factors for cardiovascular diseases (CVD) are divided into modified and unmodified ones [1]. Modified risk factors include such factors as smoking, dyslipidemia (increased LDL, triglycerides, reduced HDL), high blood pressure, diabetes, obesity, dietary factors, low level of physical activity, alcohol abuse. Unmodified risk factors are personal life history and family history [2].

Generally accepted criteria used to identify the severity of CVD risk implicate the so-called new lipid and nonlipid factors.

New lipid risk factors comprise elevated triglycerides, lipoprotein remnants, small particles of LDL, HDL subtypes, apolipoproteins B and A-I, cholesterol LDL/cholesterol HDL ratio [3].

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New nonlipid risk factors include 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), V Leidenfactor, protein C, antithrombin III); inflammatory factors; increased fasting glucose levels [4].

The study provided evidence for an important role of folate cycle gene polymorphism in the development of cardiovascular diseases. The aforementioned process can be caused by a disturbancein DNA synthesis resulting in dysregulation of proliferative processes and apoptosis [5]. Disturbancesin folate cycle are thought to be caused by genetic defects of enzymes (MTHFR, MTR, MTRR), folic acid deficiency, vitamins B6 and B12deficiency. The course of CVD is more complicated by a combination of several, even moderately expressed abovementioned risk factors as compared to one most important risk factor.

Additional risk factors for disturbances in folate cycle include gastrointestinal diseases with malabsorption of vitamin B complex (ulcerative colitis, Crohn's disease, celiac disease, enteritis, gastritis, peptic ulcer disease); malignant neoplasms of the pancreas and intestine; kidney diseases; persistent chronic infections; prolonged use of anti-

convulsants, methotrexate, metformin, H2-receptor antagonists, eufillin, folic acid antagonists, drugs interrupting the absorption of folates; factors related to lifestyle (smoking, excessive consumptionof alcohol or coffee (more than 5 cups of coffee a day); psycho-emotional stress; sedentary way of life [6, 7].

Defects of the folate cycle enzymes are accompanied by microangiopathyof various focalization, particularly "bright" hands and feet, cutis marmorata; varix dilatation. Complications associated with homocysteinuria include mental retardation, mental disorders, convulsions, skeletal disorders, osteoporosis, dislocation of the lens, myopia, iridodonesis. CNS disorders caused by brain vessels thrombosis are manifested by spastic paralysis, paresis, mental retardation and neuro-psychic signs (poor attention switching, low performance capability). Challenges presented by risk stratification are rather associated with thorough clinical examination than with scales and classifications, as it is appropriate to assess the risk for each patient and adjust ttherapeutic approach depending on the findings.

2 PURPOSES, SUBJECTS AND METHODS:

2.1 Purpose

The aim of the study was to evaluate risk stratification factors for cardiovascular diseases in children with gastrointestinal disorders.

2.2 Subjects

The study was performed at Gastroenterologyl Department of Regional Children's Clinical Hospital in Kharkov from 2015 to 2016. 66 children aged from 2 to 17 years, 32 (48.5%) girls and 34 (51.5%) boys aged 11.3±4.1 years with chronic gastrointestinal problems were examined. (chronic gastroduodenitis, duodenal ulcer, functional disorders of the biliary tract, pancreatopathy)

2.3 Methods

Diagnosis was verified by anthropometric data assessment, conventional clinical laboratory and instrumental examination (ECG, echocardiography). The original "Genetic questionnaire" was elaborated and used during the study.

Conflict of interests

There is no conflict of interests.

3 RESULTS AND DISCUSSION

Anthropometric data analysis showed normal BMI in 42.4% of the examined patients, increased BMI in 30.2% and low BMI in 24.0%. Thus, the group under investigation comprised children predisposed to obesity as well as patients with low body weight, which can be explained by loss of appetite, one of the symptoms of gastrointestinal diseases.

The most prevalent gastrointestinal diseases were 42.4% chronic gastroduodenitis, 15.2% biliary dyskinesy, 12.1% pancreatopathy and 9.1% duodenal ulcer, which corresponds to the data provided by the leading experts concerning the current situation in pediatric digestive disorders in Ukraine.

At the time of admission all the children underwent objective evaluation of the cardiovascular system (table 1).

Table 1

Data on objective evaluation of the cardiovascular system in patients with gastrointestinal diseases

Parameters	Data
Average SBP, mmHg	108.4 ± 11.05
Average DBP, mmHg	70.1 ± 7.8
Average heart rate, beats per min	82.2 ± 11.0

Thus, the analysis showed that 46 (69.7%) children hadnormal blood pressure,7 (10.6%) children had prehypertension, and 9 (13.6%) children were found to have stage 1 hypertension. Meanwile average systolic blood pressure was within a reference range. Muffled heart sounds were observed in 15 (22.7%) patients, functional systolic murmur in 25 (37.8%).

Only in 31.8% of patients ECG indices corresponded to age norms. The most frequent alterations included lengthening of the PQ interval, T wave andSTintervalchanges, lengthening of the QT interval; that is, patients were predominantly found to have ECG changes reflecting disturbances of myocardial repolarization (table 2). Evaluation of pacemaker function shown by electrocardiography revealed monotopic heart rhythm disturbances in 50% of patients.

Table 2

Changes of ECG indices in patients

Character of changesin ECG indices	% of the number of children
Lengthening of the PQ interval	57.6
Lengthening of the QRS interval	18.2
Lengthening of the QT interval	24.2
Changing of the ST interval and T wave	42.4
Monotopic heart rhythm disturbances:	50.0
– sinus arrhythmia	21.2
– sinus tachyarrhythmia	10.6
– sinus bradyarrhythmia	18.2

Thus, sinus arrhythmia observed in 21.21% of patients was the most frequent condition. According to ECG data, no organic heart disease in any of the patients was registered which was also confirmed by echocardiography.

Minor structural cardiac abnormalities included abnormal trabeculae of the left ventricle in 28.8% and mitral valve prolapse (mainly grade 1) in 24.5% (table 3).

Table 3

The incidence of minor structural cardiac abnormalities in pediatric patients

Anatomical and physiological indices	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%

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

The patients' medical records were studied in details to identify risk factors for CVS diseases.

Evaluation of patients' historyusing "Genetic questionnaire" showed that 37.9% of the patients' parents consumed more than five cups of coffee per day, 41.0% of parents smoke. Besides, 22.7% of parents were overweight, 11.4% suffered from class 1 obesity, 3.8% of parents had class 2 obesity. Type II diabetes was observed in 8.2% of parents and 18.2% other relatives. Furthermore, 36.4% of the surveyed children had sedentary lifestyle.

Thus, children with gastrointestinal disorders were found to have the following risk factors: family history burdened with early cardiovascular diseases in 41.1% of the examined children (7.6% of the respondents were diagnosed with cardiovascular diseases), 41.0% of smoking parents, overweighed or obese 30.2% of children and 37.9% of parents.

The examined patients with gastrointestinal disorders suffered from the following cardiovascular abnormalities: prehypertension in 10.6%, stage 1 hypertension in13.6%, muffled heart tones in22.7%, functional systolic murmur in 37.8%.

Echocardiography detected deviations in 68.2% of the surveyed children; pacemaker function assessment showedmonotopic heart rhythm disturbances in 50% of patients. ECG data confirmed by ECHOCG did not identify symptoms of organic heart diseases in any of the patients. Minor structural cardiac abnormalities included abnormal chordae of the left ventricle in 28.8% and mitral valve prolapse in 24.5%. Moderate dilatation of the left ventricle was observed in 30.3% of children.

The fndings, obtained by "Genetic questionnaire" revealed phenotypic changes indicative of genetic defects of folate cycle enzymes, denoted by blonde hair in 54.5% of children, blue eyes - 28.8%, pale skin - 19.7%, vascular pattern on the skin - 13.6%, visual disorders - 13.6%, hearing disorders - 1.5%, posture abnormalities - 45.5%, predisposition to fracture of bones - 15.2% of the surveyed children (table 4). These changes can indicate the presence of microangiopathies of various localization if hyperhomocysteinemia.

Table 4

Findings obtained by "Genetic questionnaire" (%)

Sign	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%
Visual disorders	13.6%	20.0%	18.8%
Hearing disorders	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%
Predisposition to fracture of bones	15.2%	3.1%	1.5%

Recognition of possible heterogeneity of these diseases provides basis for implication of the results of genetic studies in the selection and personilization of therapy and stratification of cardiovascular risk.

4 CONCLUSION

Determination of the state of the cardiovascular system in children with gastrointestinal disorders using "Genetic questionnaire" gives a possibility to stratify risk factors for the development of cardiovascular diseases.

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РЕЗЮМЕ

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СТАН СЕРЦЕВО-СУДИННОЇ СИСТЕМИ У ДІТЕЙ З ГАСТРОЕНТЕРОЛОГІЧНОЮ ПАТОЛОГІЄЮ

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В статті викладено основні підходи до стратифікації кардіоваскулярного ризику у дітей с гастоентерологічноюпатологією. Зроблено акцент на немодифікованихфакторах ризику, виявлених за допомогою «Генетичного опитувальника». Визначена роль поліморфізму генів фолатного циклу у розвитку серцево-судинних захворювань у дітей.

Ключові слова: кардіоваскулярний ризик, діти, серцево-судинна система,гастоентерологічна патологія.

РЕЗЮМЕ

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СОСТОЯНИЕСЕРДЕЧНО-СОСУДИСТОЙ СИСТЕМЫ У ДЕТЕЙ С ГАСТРОЭНТЕРОЛОГИЧЕСКОЙ ПАТОЛОГИЕЙ

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В статье изложены основные подходы к стратификации кардиоваскулярного риска у детей с гастоэнтерологической патологией. Сделан акцент на немодифицированных факторах риска, выявленных с помощью «генетической опросника». Определена роль полиморфизма генов фолатного цикла в развитии сердечно-сосудистых заболеваний у детей.

Ключевые слова: кардиоваскулярный риск, дети, сердечно-сосудистая система, гастоэнтерологическая патология.

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