Inter Collegas

Experientia docet

2016

N1(3)

INTER COLLEGAS JOURNAL

2016

Vol. 3 No.1

OFFICIAL JOURNAL OF
KHARKIV NATIONAL MEDICAL UNIVERSITY
ISSN 2409-9988

Recommended for publishing
by Scientific Council of
Kharkiv National Medical
University

"___" _____ 201__

Correspondence address:
61022, Kharkiv,
Nauki Avenue, 4
e-mail: collegas@ukr.net
URL:
http://inter.knmu.edu.ua/pub

Periodicity:
4 times a year

INTER COLLEGAS JOURNAL, VOL. 3, No. 1 (2016)
ISSN 2409-9988

Table of Contents

PEDIATRICS

DERMATOLOGY

INTER COLLEGAS JOURNAL, VOL. 3, No. 1 (2016)
ISSN 2409-9988

OBSTETRICS and GYNECOLOGY

PEDIATRICS

T.V. Frolova, O.V. Ohapkina, I.I. Tereshchenkova, I.R. Siniaieva

IMPACT OF ENVIRONMENTAL FACTORS ON THE LEVEL OF PHYSICAL GROWTH AND DEVELOPMENT OF CHILDREN IN KHARKIV REGION

Kharkiv National Medical University, Ukraine

Abstract: The study deals with determination of the level of physical development in 2600 children who live in different areas of ecological well-being of Kharkiv region. Children living in environmentally disadvantaged areas were found to have accelerated linear growth, and the degree of an increase in this index depends on incorporation rate of conditionally toxic microelements (r=0.72). The study identified gender-specific impact of environmental factors on children's body weight. Body weight indices in boys living in environmentally disadvantaged areas were shown to be below age norms, whereas in girls a decrease in these indices was observed in environmentally favorable areas. Environmental deterioration results in imbalanced and impaired cycle of physical development, which has a negative effect on health in general.

KeyWords: children, physical development, ecology.

INTRODUCTION

Low resistance to harmful environmental factors in children has recently become the focus of great concern for medical community [1-2]. Despite a recent significant decline in Ukrainian industry, air pollution remains a pressing challenge. Road transport is regarded as one of the greatest sources of pollution with its overall emission of harmful substances in the air reaching 52%. Some scientists suggest that physical growth of children depends on the extent of environmental pollution – moderate pollution activates acceleration and high degree of pollution leads to growth rate reduction in children [3].

Physical growth and development (PGD) in children are known to be one of the main objective indices of general health. Main PGD criteria include weight, height, head and chest circumference et cetera. Growth and development were shown to have a nonlinear dependence on the child's age, but it is necessary to consider that these processes reflect physiological or pathological processes occurring in the body.

Corresponding Author:
***Olga Ohapkina**, MD, PhD, Professor, Department of Propedeutic Pediatrics No. 1, Kharkiv National Medical University, Ukraine. E-mail: ohapki@mail.ru*

Given the impact of environmental factors on the child's PGD indices, monitoring of PGD changes helps to analyze the reactions of the growing organism to exogenous factors. Moreover, follow-up control of the impact of environmental factors on PGD is effective in elaboration and administration of preventive measures against PGD impairment.

2 PURPOSES, SUBJECTS AND METHODS:

2.1 Purpose

The aim of the study was to establish growth rate characteristics of anthropometric indices in children and adolescents in relation to the environmental conditions of the area of residence.

2.2 Subjects

The method of expeditionary examinations of organized groups was used to examine 2600 children at the age rating from 7 to 17 years old, permanently residing in Kharkiv region. Groups of children were stratified on the basis of age, sex and environmental characteristics of the area of their residence. Thus, the

environmentally favourable area, where there are no large industrial enterprises, included 676 children (group I); relatively unfavourable areas, where the average power level enterprises, of mainly agricultural directionprevail included 1291 children (group II) and environmentally unfavourable areas with large industrial complexes and a large number of road transport included 633 children (group III).

2.3 Methods

The method of expeditionary survey of organized groups was used to examine 2600 children aged 7-17 years, permanently residing in Kharkiv region. The groups were divided according to the age, sex and environmental characteristics of the area of residence. Thus, 676 children (group I) lived in environmentally favorable areas without large industrial enterprises; while 1291 children (group II) lived in relatively unfavorable areas with medium power enterprises, mainly agricultural; 633 children (group III) resided in environmentally unfavorable areas with large industrial complexes and a considerable amount of road transport emissions. The program of expeditionary survey of the representative number of children implied clinical and history study, anthropometry, assessment of alimentary provision of nutritional homeostasis, determination of essential and conditionally toxic microelements in hair by mass spectrometry with inductively coupled plasma using "ElvaX" device (2008). Hair was selected as a biological material due to its exceptionally informative nature reflecting the exposure to microelements. ME status examination involved only the children who did not take vitamins or mineral substances for the last 2 months prior to the study.

Statistical analysis was carried out using parametric and non-parametric criteria (Student-Fischer test, Van-der-Waerden test, etc.), probability distribution of characteristics and correlation analysis.

The study was conducted according to the international biotic standards.

Conflict of interests

There is no conflict of interests.

3 RESULTS AND DISCUSSION

Evaluation of mineral composition of hair showed that microelement profile of group I children was characterized by an impaired balance of essential macro- and microelements (ME), namely calcium, magnesium and zinc secondary to a slight increase in cobalt, chromium and strontium (to not more than 15%). In group II children ME disorders resulted from an increase in conditionally toxic microelements with an increase in strontium by 20% and lead by 13%. Group III children were found to have a significant shortage of essential abovementioned ME and accumulation of strontium to more than 40%, lead to 30%, aluminum to 30% and other conditionally toxic microelements.

Assessment of PGD in children of Kharkiv region at large showed a reduction in growth rates which may be explained by significant socio-economic difficulties of the last decade, namely dietary intake quality deterioration, unbalanced and irregular meals, reduced motor activity of children and adolescents, etc.

The study of the growth rates in groups under investigation identified marked gender-specificity of the environmental impact. Thus, the increase in linear growth in boys of all ages was significantly higher in group III children than in children of groups I and II ($p < 0.05$) and a similar dependence was observed in boys of the group II and group I ($p < 0, 05$) (Table 1).

Thus, boys, permanently residing in environmentally unfavorable conditions show acceleration in linear growth indices, and its degree depends on the extent of conditionally toxic ME accumulation ($r = 0.72$), due to biostimulating heterosis-like effect of industrial chemicals polluting the environment.

Table 1.

Age-sex height changes (cm) of children living in Kharkiv region

group/sex	I group		II group		III group	
Age	girls	boys	girls	boys	girls	boys
7 years old	120.3	120.5	121.6	121.5	118.3	122.4
8 years old	125.0	123.9	128.1	127.0	122.6	1349
9 years old	134.8	126.0	132.6	131.5	125.7	138.8
10 years old	139.7	127.5	137.3	137.4	139.9	142.8
11 years old	143.6	134.9	142.5	142.8	144.6	148.9
12 years old	152.5	138.7	147.0	147.4	151.5	152.5
13 years old	159.9	142.8	153.5	156.2	157.9	160.8
14 years old	166.5	149.8	161.1	159.2	166.0	163.0
15 years old	166.7	156.8	166.9	160.9	169.8	164.5
16 years old	169.8	160.3	173.1	164.2	174.1	168.3
17 years old	171.8	163.8	175.9	168.8	177.6	176.1

Assessment of linear growth indices in girls aged 7-14 years living in different ecological conditions did not reveal any significant differences. An increase in this index was also observed in group III girls. However, in puberty, at the age from 15 to 17 years, girls of groups I and III were found to have significant differences in growth indices, with an increase in this index in girls from environmentally unfavorable areas ($p < 0.05$).

Evaluation of body weight changes indicated an absence of distinct gender relation as opposed to growth. Thus, boys under 11 and girls under 16 were shown to have no significant differences in the dependence of body weight indices on the environmental characteristics of the area (Table 2). It should be noted that body weight indices in boys of this age were slightly higher among group I boys than in boys of groups II and III ($p > 0.05$). Besides, body weight in boys in puberty living in environmentally unfavorable areas was below age norms compared to PGD in children living in Kharkiv region.

Table 2.

Age-sex changes in body weight (kg) of children living in Kharkiv region

group/sex	I group		II group		III group	
Age	girls	boys	girls	boys	girls	boys
7 years old	24.5	21.7	24.7	25.0	24.3	23.3
8 years old	28.5	27.7	29.5	26.8	27.9	28.9
9 years old	31.7	31.4	31.2	27.8	30.2	29.0
10 years old	35.0	34.6	34.4	33.0	34.8	35.2
11 years old	39.5	43.2	37.3	37.5	40.2	36.2
12 years old	45.0	46.9	42.5	42.3	47.0	40.1
13 years old	50.0	52.4	49.6	48.3	49.3	45.6
14 years old	52.3	58.6	52.0	51.3	53.8	50.4
15 years old	56.9	64.0	56.5	52.9	56.3	57.5
16 years old	58.0	67.3	59.4	62.0	66.1	54.8
17 years old	60.7	68.8	66.5	64.0	68.8	56.4

As for girls in puberty, it should be mentioned that weight indices in group I girls were lower than the corresponding indices in group III girls ($p < 0.05$), whereas body weight in 17-year-old girls of group I was slightly lower as opposed to group II girls ($p < 0.05$).

Proper PGD is known to be characterized by cyclicity with accumulation of body weight prior to an increase in linear growth, which primarily provides good health in general. Evaluation of PGD growth rate in children under investig - tion showed a significant impact of environmental factors on PGD cyclicity. Thus, the largest increase in body weight in group I children was observed in 12-year-old girls and 11-year-old boys ($p < 0.05$). Alternatively, the maximum increase in height was observed in 14-year-old girls and 13-year-old boys ($p < 0.05$). Consequently, PGD processes in children permanently residing in areas of conventional environmental well-being relate to age criteria of the child's development.

The maximum increase in body weight in group II children was observed in 16-year-old boys and 17-year-old girls. However, the highest increase in linear growth in boys was observed at the age of 13 years ($p < 0.05$), and in girls at the age of 14 years ($p < 0.05$), which may be regarded as a pathological basis for further PGD of the child. Disruption

of PGD cyclicity in group II children comprised 4 ± 0.35 years on average ($p < 0.05$).

The most unfavorable PGD was observed in group III boys, with the maximum increase in body weight at the age of 15 years (it made up not more than 15% on average, $p < 0.05$), and the maximum increase in linear growth index at the age of 13 years (it made up 12% on average, $p < 0.05$) and at the age of 17 years old (it made up 12% on the average, $p < 0.05$), which indicates a distinct imbalance in the whole PGD process in boys permanently residing in envir-?nmentally unfavorable areas of Kharkiv region. The maximum increase in body weight in group III girls was observed at the age of 16 years (it made up 20% on average, $p < 0.05$), the maximum increase in linear growth occurred at the age of 10 years (it made up 20% on average, $p < 0.05$). This disruption of PGD cyclicity in girls of this group made up 6 ± 0.4 years on average ($p < 0.05$), which certainly conditioned its impact on physical health of children.

Environmental deterioration can lead to an imbalance of certain PGD indices, which definitely affects general health of children and requires elaboration of a framework of preventive measures.

4 CONCLUSIONS

1. Children permanently residing in unfavorable environmental conditions were found to have an increase in linear growth indices, which can be explained by biostimulating heterosis-like effect of industrial chemicals polluting the environment.
2. The degree of growth indices acceleration in children correlates with the degree of accumulation of conditionally toxic microlements ($r = 0.72$).
3. Body weight indices in boys in puberty living in ecologically unfavorable areas were slightly lower than the age norms for physical development of children in Kharkiv region, whereas these indices were lower in girls living in environmentally favorable areas.
4. Environmental deterioration leads to an imbalance of physical processes and deregulation of cyclic processes of body weight accumulation and linear growth rates.

REFERENCES

1. A.N. Stozharov (2007) Medical ecology, Minsk: Higher education institution, 265.
2. T.V. Frolova, O.V. Ohapkina, N.F. Stenkova, O.P. Medvedeva (2012) Peculiarities of formationof population health in children in environmental conditions,Child's health, 2 (37), 24-27.
3. A.A. Baranov, V.R. Kuchma, N.A. Skoblina (2008) Physical development of children and adolescents at the turn of Millennium, M.: Publisher: Scientific Center of Children's Health, Russian Academy of Medical Sciences. 2008, 216.

РЕЗЮМЕ

Фролова Т.В., Охапкіна О.В., Терещенкова І.І., Сіняєва І.Р.

ЕКОЛОГІЧНИЙ ВПЛИВ НА РІВЕНЬ ФІЗИЧНОГО РОЗВИТКУ ДІТЕЙ ТА ПІДЛІТКІВ ХАРКІВСЬКОГО РЕГІОНУ.

У роботі наведені результати дослідження рівня фізичного розвитку 2600 дітей, які мешкають у різних екологічних умовах харківського регіону. Встановлено, що у дітей з несприятливо екологічних районів відбувається прискорення лінійного зросту, а ступінь прибавки цього показника у дитячому віці має кореляційну залежність від ступеню накопичення умовно-токсичних мікроелементів ($r=0,72$). Виявлені певні гендерні особливості впливу екологічних факторів на показники маси тіла дітей. Так, у хлопчиків мешканців екологічно несприятливих районів маса тіла нижче вікових нормативів, тоді як у дівчаток нижчі показники маси тіла спостерігаються у мешканців екологічно сприятливих районів. Погіршення екологічного становища призводить до дисбалансу та порушення циклічності фізичного розвитку, що негативно впливає на рівень здоров'я в цілому.

Ключові слова: діти, фізичний розвиток, екологія.

РЕЗЮМЕ

Фролова Т.В., Охапкина О.В., Терещенкова И.И.,
Синяева И.Р.

ВЛИЯНИЕ ЭКОЛОГИИ НА УРОВЕНЬ ФИЗИЧЕСКОГО РАЗВИТИЯ ДЕТЕЙ И ПОДРОСТКОВ ХАРЬКОВСКОГО РЕГИОНА

В работе представлены результаты исследования уровня физического развития 2600 детей, которые проживают в разных по экологическому благополучию районах харьковского региона. Установлено, что у детей, проживающих в экологически неблагоприятных районах, происходит ускорение показателей линейного роста, а степень прибавки данного показателя зависит от степени накопления условно-токсических микроэлементов (r=0,72). Установлены гендерные особенности влияния экологических факторов на показатель массы тела детей. Так, у мальчиков, проживающих в экологически неблагоприятных районах, показатели массы тела ниже возрастных нормативов, тогда как у девочек снижение этих показателей отмечается в экологически благоприятных районах. Ухудшение экологического состояния приводит к дисбалансу и нарушению цикличности физического развития, что негативно влияет на состояние здоровья в целом.

Ключевые слова: дети, физическое развитие, экология.

Received: 01-Feb. – 2016
Accepted: 20-Mar. - 2016

PEDIATRICS

M.O. Gonchar, T.B. Ishchenko, V.A. Koval

MAIN FEATURES OF LEUKEMOID REACTIONS IN CHILDREN

Kharkiv National Medical University, Ukraine

Abstract: Leukemoid reactions are abnormal reverse reactions of blood with morphological signs similar to leukemic or sub-leukemic manifestations, but with different pathogenesis of these hematological changes.The article presents cur-rent views on etiology, pathogenesis, presentation and clinical manifestations in relation to etiological factors, diagnosis guidelines and differential diagnosis of leukemoid reactions in children, as well astherapeutic approach in these conditions..

KeyWords: leukemoid reactions, children, infections

INTRODUCTION

Leukemoid reaction (LR) is a secondary symptomaticreversible change of the "white blood" in response to a stimulus. So it is a reactive, functional condition of hematopoietic, lymphatic and immune systems secondary to various diseasesaccompanied by the development of immature white blood cellsin the peripheral blood, which numbermay exceed 50000 per 1 mm3. Thus, LR is an abnormal reaction of blood with morphological signs similar to leukemic or subleukemic manifestations, but with different pathogenesis of these hematological changes.

As reactive changes in blood are similar to hematological malignancies, it is important to differentiate themfrom leukemia. The causes of leukemoid reactions are usually evident with marked clinical signs (e.g., inflammation). Changes in blood are transient and blood levels return to normal when the causes disappear. There are no signs of inhibition of normal hematopoiesis.

• *Corresponding Author:*

***Tatiana Ishenko**, MD, PhD, Associate Professor, Department of Pediatrics 1 and Neonatology, Kharkiv National Medical University, Ukraine. E-mail: tanyatb@mail.ru*

Due to general consistent patterns and presentation of certain leukemoid reactions, their basic differences from leukemia are as follows: leukemoid reactions are mostly triggered by bacterial or viral infections, emergency stress irritants and also by variousbacterial and nonbacterial pathogens, causing sensitization.

Etiology and pathogenesis

Leukemoid reactions of myeloid type develop in various infectious and noninfectious processes, septic conditions, endogenous and exogenous intoxications, severe injuries and acute hemolysis. They can particularly be observed in various infections (sepsis, tuberculosis, purulent processes, lobar pneumonia, scarlet fever, mumps, dysentery), intoxication (therapeutic intoxication, including sulfanilamide drugs, azotemia, uremia), Chlamydia, metastatic tumors of the bone marrow, ionizing radiation (radiotherapy).

Leukemoid reaction of lymphocytic and lymphomonocytictypes can be observed in infectious mononucleosis, whooping cough, chicken pox, scarlet fever, rubella, tuberculosis, poisoning. Individualreactivity in children plays a great role in the development of leukemoid reactionswith the exception of specific factors (viruses, helminths, toxins, infectious agents).

It should be noted that development of solid tumors is also often accompanied by neutrophilic leukemic reactions accompanied by thrombocytosis, thrombocytopenia and

erythrocytosis.

The main link in LR pathogenesis is activation of normal hematopoiesis and excessive blood cells output toperipheral blood (reactive hyperplasia of leukopoietic tissue) and output of immature blood cells into peripheral blood.

Classification

Leukemoid reaction can be classified according to the course of the diseaseand the type of irritation hematopoietic lineage of the bone marrow.

According to the course of the disease LRsare divided into:

- Phase of expressed manifestations
- Phase of recession
- Phase of normalization with trace reactions

Accordingto the type of irritation hematopoietic lineage of the bone marrow LR sare divided into:

1. Reactions of myeloid type
1.1. Neutrophilicleukemoid reactions
1.2. Eosinophilic leukemoid reactions
2. Reactions of lymphoidtype
2.1. Lymphomonocyticleukemoid reactions
2.2. Lymphocytic leukemoid reactions
2.3. Plasmocyticleukemoid reactions
2.4. Leukemoid reaction with blast cells
3. Secondary (reactive) thrombocytosis
4. Secondary erythrocytosis
5. Mixed forms of leukemoid reactions
6. Rare forms of leukemoid reaction
6.1. Cytopenia
6.2. Leukemoid reactions of basophilic type

The main clinical manifestations of leukemoid reactions and diagnostics

Clinical presentation depends on the underlying disease that triggered leukemoid reaction.

Leukemoid reactions are basically characterized by a high level of white blood cells in peripheral blood (with the exception of cytopenic leukemoid reaction) and a distinct shift in white blood count with singular blast cells.

Leukemoid reactions of myeloid type differ from moderate leukocytosis – often to 12.0-30.0×109/l and a subleukemic shift in leukogram to myelocytes, sometimes to myeloblasts (myeloblastic type). Leukemoid disorders may be observed in blood count without significant leukocytosis, and vice versa – mild abnormalities in leukogram with stab and singular metamyelocytes inincreased leukocytosis (40.0-50.0×109/l). Leukemoid reaction of lymphoid type is characterized by moderate leukocytosis with absolute lymphocytosis (up to 70-90%). Other hematologic parameters usually do not undergo significant changes.

Diagnosis is based on presenting clinical signs of the underlying disease, with possible reaction and absence of symptoms of leukemic process. Absence of blasts in the peripheral blood in patients with severe leukocytosis (30.0-50.0×109/l and higher) practically excludes hemoblastosis. In diagnostic difficulty patients are referred for examination of bone marrow and lymph node aspirates.

Reactions of myeloid type are characterized by a shift to the left – from an increased number of stab cells to singular blast cells with presence of all intermediate forms. The level of hyperleukocytosis and the shift of blood count do not always correspond to the severity of the underlying disease, but depend on the response of the hematopoietic system to the infectious and toxic effects. Bone marrow aspirate most often shows an increase in immature granulocytes and irritation of myeloid lineage.

Neutrophilic leukemoid reactions develop in the following cases:

- Infections - sepsis, scarlet fever, purulent processes, diphtheria, lobar pneumonia, tuberculosis, dysentery, etc.;
- Exposure to ionizing radiation;
- Injuries of the skull;
- Intoxication (uremia, CO poisoning);
- Bone marrow metastases of malignant tumors
- Lymphogranulomatosis;
- Steroid hormones therapy.

Eosinophilic reactions ("high eosinophilia") develop in allergic processes or in diseases with allergies, as well as in parasitic diseases. They are characterized by the development of a great number of eosinophils (90%

leukocytosis at 100×109) and eosinophils may show excessive segmentation of nuclei.

Prognostic assessment of eosinophilic leukemic reaction is equivocal: in infections it can be considered as an evidence of immune responses,in collagen disease it can be regarded as an unfavorable sign; in parasitic and helminth diseases eosinophilia does not determine features of their course.

Lymphomonocytic leukemoid reactions develop in infectious mononucleosis (Filatov and Pfeifferdisease). It was first described in 1885 by a pediatrician N.V.Filatov. It is a disease of viral etiology. Infectious mononucleosis begins acutely with a sudden rise in temperature that persists at 39-39.5^{0}C during the day. Sometimes fever is preceded by prodromal signs: malaise, myalgia, dizziness, and systemic lymphadenopathy that subsides in 10-15 days, but slight enlargement and tenderness of lymphatic nodes may be observed for several weeks, sometimes months. Subsequently patients develop enlargement of the spleen and sore throat with necrotic changes. At the middle stage of the disease patients are found to have leukocytosis (10.0-25.0×109/l). Leukogram shows 50-70% of lymphocytes with high percentage of monocytes (12 to 40-50%). Commonly there are atypical mononuclear cells, called "lymphomonocytes" (cells are larger than lymphocytes, but smaller than monocytes, with monocytic form of nucleus and intensively basophilic cytoplasm). Lymphomonocytes are modulated T- and NK-lymphocytes, which get to the bloodstream by initiation of B-lymphocytes. Mild anemia, sometimes slight thrombocytopenia and neutropenia are also observed.

Atypical mononuclear cells (reactive lymphocytes) are transformed lymphocytes, mostly reactive T-cells that provide antiviral protection and proliferative B-lymphocytes.

Atypical mononuclear cells are common not only in infectious mononucleosis. In health their number is 1/6 of the number of lymphocytes. The number of atypical mononuclear cells can be increasedin any viral infection (acute respiratory viral infections, influenza, hepatitis, cytomegalovirus infection, herpes and pediatric infections), other infections (yersiniosis, toxoplasmosis, chlamydia), vaccination, autoimmune diseases, drug intolerance, tumors.

Lymphocytic leukemoid reactions (infectious lymphocytosis) develop in acute viral and bacterial infections and are characterized by leukocytosis with absolute lymphocytosis, an increased level ofprolymphocytesin the bone marrow (in peripheral blood they are absent).

Plasmocytic leukemoid reactions occur in diseases caused by protozoa (toxoplasmosis), viral infections (chickenpox, measles, rubella), et cetera. Increased level of plasma cells (2%) in splenomegaly, blood and bone marrow is typical for this type of leukemoid reactions.

Leukemoid reactions with blast cells develop in severe viral infections (cytomegalovirus, etc.). As for blast cells, blast transformation of B-lymphocytesmay be observed in the bone marrow, lymph nodes and peripheral blood.

Secondary absolute erythrocytosis is caused by increased erythropoiesis, relative hemoconcentration and polycythemia. Plasma volume is typically decreased. It is characterized by increased levels of red blood cells, hemoglobin and erythropoietin.

Thrombocytosis (platelet count more than500×109/l) may be primary, as a result of tumor proliferation of megakaryocytes in chronic myeloproliferative diseases (essential thrombocythemia, idiopathic myelofibrosis, chronic myeloid leukemia), and secondary, reactive. Symptomatic (reactive) thrombocytosis is possible in malignant tumors, inflammatory diseases, following bleeding, hemolytic crises, after surgical operations and splenectomy. Secondary thrombocytosis is usually not as distinct as primary one and is rarely complicated by thrombosis (or bleeding) disappearing after elimination of the cause.

Leukemoid reactions to the tumor can becharacterized by irritation of one lineage of hemopoiesis,(e.g., neutrophilia, monocytosis, eosinophilia, erythrocytosis or thrombocytosis) or with irritation of several lineages of hemopoiesis – mixed leukemoid reactions (neutrophilia and thrombocytosis, erythrocytosis and monocytosis, or other combinations). Signs of myelemia ("bone marrow in the blood") are observedinmiliary metastasestothe bone marrowwith neutrophilia and significant left shiftto myelocytes, promyelocytes and blasts. The number of leukocytes in this case varies from severe leukopenia to hyperleukocytosis. Patients are usually found to have evident anemia with reticulocytopenia and thrombocytopenia. Similar signs can be observed in acute erythroleukemia (AML-M6) and acute immune hemolysis. Diagnosis is obvious in detecting cancer cells in bone marrow aspirate or trepanobiopsy.

Leukemoidreaction with cytopenia is a rare form of myeloid reaction, when patients have a left shift in white blood count to singular immature forms secondary to leukopenia (1500-2500 leukocytes per 1 ml of blood). In such cases blood picture resembles chronic myeloid leukemia and myelofibrosis.

Leukemoid reactions of basophilic type are rare. Reactive basophilia may develop in allergic reactions, hemolytic anemia, ulcerative colitis, hypothyroidism, leukemia.
Hematological diseases such as chronic myeloid leukemia, Hodgkin's disease are characterized by eosinophilic and basophilic associations.

Differential diagnosis

As reactive changes in blood are similar to leukemia, it is necessary to provide differential diagnosis (Table 1). It is generally important to consider that typical signs of tumor progression inherent to leukemia are not detected inleukemoid reactions, so metaplastic anemia and thrombocytopenia are not observed. As in leukemia, distinct immaturities of the peripheral blood to the extent of development of blast cells occur secondary to leukemoid reaction.

Table 1

The main criteria for differential diagnosis of leukemoid reactions and leukemia

	Leukemoid reactions	Leukemia
Causes	Infectious agents, biologically active substances, products of tissue destruction	Carcinogens
Pathogenesis	1. Activation of normal hematopoiesis and excess of formed elements in blood flow (reactive hyperplasia of leukopoietic tissue) 2. Exit of immature leukocytes into the bloodstream	The transformation of normal haematopoietic cells to a tumor
The bone marrow Peripheral blood	Focal hyperplasia of normal hematopoietic cells in proliferative reactions. The presence of blast and immature forms of leukocyte, platelet and erythrocyte hematopoiesis in the proliferative reactions. Usually leukocytosis is present. Rarely - leuko-, erythro-, thrombocytopenia is present. Signs of degeneration of formed elements	Generalized hyperplasia of tumor of heamatopoietic cells Cytopenia or increased level of leukocytes is combined with the presence in the blood of leukemic blast cells. Leukemic breakdown in acute leukemia. Signs of degeneration of cells are usually absent.
Duration	It is temporary, reversible and it is not transformed to leukemia	It is saved during the disease

But in most cases of leukemoid reaction, except leukemoid reaction with blasts, the number of blast elements in peripheral blood does not exceed 1-2%. It should be noted that in differential diagnosis of leukemoid reactions they usually develop on the background of severe patient's condition. Splenomegaly is not typical for leukemoid reactions and toxic granulation, vacuolization of nucleus and cytoplasm and even intravital disintegration of the nucleus may be found in neutrophil cytoplasm. Normal cellular composition of the bone marrow is indicative of leukemoid reaction.
Moreover, rapid normalization of peripheral blood occurs after elimination of the main etiological factor, which does not take place in hemoblastosis.

Therapeutic approach to leukemoid reactions in children

Prognosis of leukemoid reactions depends on the underlying disease. In most cases prognosis is favorable.

Specific therapy is generally not required. In most cases patients require treatment of the underlying disease and associated leukemic reaction.

Conflict of interests

There is no conflict of interests.

REFERENCES

1. Zhavoronok T.V. (2010). Uchastie sistemy glyutationa v podderzhanii funkcional'nogo sostoyaniya nejtrofilov pri ostrom vospalenii. Byulleten' sibirskoj mediciny, 5, 28–32.

2. Korotina O.L., Generalov I.I. (2012). Nejtrofil'nye vnekletochnye lovushki: mekhanizmy obrazovaniya, funkcii. Immunologiya, allergologiya, infektologiya, 4, 23–32.

3. Shalom G, Sion-Vardy N, Dudnik J, Ariad S. (2010). Leukemoid reaction in lung cancer patients. Israel Medical Association Journal, 12(4), 255–256.

4. Hurtado-Cordovi J, Avezbakiyev B, Frieri M, Freedman L, Gebre W. (2012). Cutaneous inflammatory malignant fibrous histiocytoma presenting with a leukemoid reaction: a case report and review of the literature. Case Reports in Medicine, 2012, 1-5. doi: 10.1155/2012/798629.

5. Hurtado-Cordovi J, Pathak P, Avezbakiyev B, Frieri M. (2012). Inflammatory malignant fibrous histiocytoma associated with leukemoid reaction or leukocytosis: a comprehensive review. International Scholarly Research Notices Oncology, 2012, 1-17. doi:10.5402/2012/946019.

6. Granger JM, Kontoyiannis DP. (2009). Etiology and outcome of extreme leukocytosis in 758 nonhematologic cancer patients: a retrospective, single-institution study. Cancer, 115(17), 3919–3923. doi: 10.1002/cncr.24480.

7. Sakka V, Tsiodras S, Giamarellos-Bourboulis EJ, Giamarellou H. (2006). An update on the etiology and diagnostic evaluation of a leukemoid reaction.European Journal of Internal Medicine, 17, 394–398.

РЕЗЮМЕ

Гончарь М.О., Іщенко Т.Б., Коваль В.А.

ОСНОВНІ ХАРАКТЕРИСТИКИ ЛЕЙКЕМОЇДНИХ РЕАКЦІЙ У ДІТЕЙ

Харківський національний медичний університет

Лейкемоїдні реакції – це патологічні зворотні реакції крові, при яких морфологічна картина має подібність до лейкемічних або сублейкемічних проявів, але патогенез цих гематологічних змін є різним. У статі представлені сучасні погляди на етіологію, патогенез, особливості перебігу та клінічні прояви в залежності від чинника виникнення, основи діагностики та диференційної діагностики лейкемоїдних реакцій у дітей, а також на лікарську тактику при цих станах.

Ключові слова: лейкемоїдні реакції, лейкоз, діти, інфекції

РЕЗЮМЕ

Гончарь М.А., Ищенко Т.Б., Коваль В.А.

ОСНОВНЫЕ ХАРАКТЕРИСТИКИ ЛЕЙКЕМОИДНЫХ РЕАКЦИЙ У ДЕТЕЙ

Харьковский национальный медицинский университет

Лейкемоидные реакции - это патологические обратные реакции крови, при которых морфологическая картина имеет сходство с лейкемическими или сублейкемическими проявлениями, но патогенез этих гематологических изменений различен. В статье представлены современные взгляды на этиологию, патогенез, особенности течения и клинические проявления в зависимости от фактора возникновения, основы диагностики и дифференциальной диагностики лейкемоидных реакций у детей, а также на врачебную тактику при этих состояниях.

Ключевые слова: лейкемоидные реакции, лейкоз, дети, инфекции

Received: 23-Feb. – 2016
Accepted: 25-Mar. - 2016

PEDIATRICS

M.O. Gonchar, N.V. Konovalova, G.R. Muratov

Mechanisms of myocardial remodeling in adolescents with hypothalamic syndrome of the puberty and arterial hypertension.

Kharkiv National Medical University, Ukraine

Abstract: The study deals with the assessment of patterns of left ventricular myocardial remodeling in adolescents with hypothalamic syndrome of puberty and arterial hypertension depending on endothelial nitric oxide synthase gene polymorphism in intron 4 (4b, 4a) and blood serum homocysteine level.

Key Words: gene polymorphism, endothelial NO-synthase, homocysteine, adolescents, myocardial remodeling, arterial hypertension.

INTRODUCTION

An increase in the number of younger patients with arterial hypertension (AH), which ranks high in the incidence and remains a significant medical and social challenge, has been observed recently [1-3]. Leading experts emphasize that determination of abnormal tendencies to the development of hypertension in adolescents, early diagnosis and correction of cardiovascular disorders exert a positive impact on the health of adults [4-8].

Hereditary factors have lately acquired certain significance among the causes of risk factors for hypertension and its complications. Mapped candidate genes, namely: angiotensin gene (AGT), angiotensin-converting enzyme gene (ACE) and endothelial nitric oxide synthase gene (eNOS) have become a prime focus for experts.AGT gene polymorphismis associated with high blood pressure in adults and left ventricular hypertrophy [9].

• ***Corresponding Author:***

***Margaryta Gonchar**, MD, PhD, Professor, Head of the Department of Pediatrics 1 and Neonatology, Kharkiv National Medical University, Ukraine. E-mail: margarytagonchar@gmail.com*

Particular attention has recently been given to the study of complications resulting from hypertension, particularly impairment of the target organs (heart, blood vessels; potential risk factors for cardiovascular complications presently include hyperhomocysteinemia [10, 11].

The mechanisms of hypertension development in overweight adults are well understood. Adaptation and subsequent chronic compensatory hypofunction of the myocardium in patients with obesity leads to an increase in myocardial mass, which can enlarge due to hypertrophy of myocardiocytes. At the same time, the increase of the heart mass in patients with obesity can be associated with the increase in itscontent of fibrous tissue. Activation of myocardial fibrosis promotes an increase in the rigidity of the walls of the left ventricle reducing myocardial ability to relax, which triggers the development of diastolic dysfunction. Besides, myocardial fibrosis results in depletion of the vascular bed of the coronary arteries and a gradual decrease in myocardial contractility, remodeling of the left ventricle with subsequent development of circulatory failure [12,14].

Development of hypertension in adolescents has been actively studied [13]. Hypothalamic syndrome of puberty (HSP) is one of the diseases occurring in most patients with hypertension. This syndrome basically involves impairment

of the system hypothalamus-hypophysis-peripheral endocrine organs with the development of insulin resistance with lipid metabolism shifts and progression of obesity. HSP is not a rare abnormality, but it is rarely diagnosed, therefore it is appropriate to study pathophysiological mechanisms underlying the formation of arterial hypertension in adolescents with HSP, presentation of metabolic disorders and methods of early diagnosis.

In view of the above, early identification of changes in the cardiovascular system in adolescents with HSP is relevant in childhood, when the groundwork for disease development or preservation of health in adults isformed [10, 11].

2 PURPOSES, SUBJECTS AND METHODS:

101 adolescents with HSP aged 14 to 17 years (average age 15.8±0.66 years) were examined at Communal Health Protection Institution "Regional Children's Clinical Hospital" and Department of Pediatrics No.1 and Neonatology due to past history of high blood pressure episodes.

The study involved assessment of case histories and presentation, physical development with waist measurement (WM), hip measurement (HM), abdominal obesity (WM/HM ratio), and body mass index (BMI). The diagnosis was specified by 24-hour blood pressure monitoring (ABPM) using MD plus unit (Russia, Novosibirsk). The state of cardiovascular system was evaluated by Doppler echocardiography with standard technique recommended by the Association of Echocardiography [1].

Polymorphism of endothelial nitric oxide synthase gene was studied by polymerase chain reaction. Homocysteine level inblood serum in patients with different genotype was evaluated by immunoenzyme assay (ELISA). Statistical data processing was carried out using STATISTICA-6 software with parametric and nonparametric methods.

Conflict of interests

There is no conflict of interests.

3 RESULTS AND DISCUSSION

The examination of 101 adolescents with hypothalamic syndrome of puberty showed the following genotypes: genotype 4b4b in 47 (46.53±4.99%) children, genotype 4b4a in 43 (42.57±4.95%) adolescents and genotype 4a4a in 11 (10.89±3.12%) teenagers.

The relation of certain biochemical indices to patient's genotype was assessed by a dispersive analysis version, namely Kruskall-Wallis test.

The study revealed statistically reliable differences in a number of indices in patients with various genotypes, particularly insulin ($p<0.05$), homocysteine ($p<0.001$), triglycerides (TG) ($p<0.05$),very low density lipoproteins(VLDL) ($p<0.05$), average systolic blood pressure during the night(ASPP(n)) ($p<0.05$), increase in the thickness of the posterior wall of the left ventricle in percent (%PWLV) ($p<0.05$), glomerular filtration rate (GFR) ($p<0.05$) (Table 1).

Table 1

The metabolic and structurally functional indicators depending on the genotype.

Parameters	genotype 4a4a (n=11)			genotype 4b4a (n=43)			genotype4b4b (n=47)			P
	Me	LQ	UQ	Me	LQ	UQ	Me	LQ	UQ	
Insulin, ulU/ml	33,2	16,52	40,08	14,68	10,4	19,9	16,2	12,8	22,46	<0,05*
Homocysteine, mcmole/l	2,9	2,5	4,6	12,2	7,9	19,3	11,8	6,9	17,3	<0,001*
TG, mmol /l	1,41	1,18	1,64	1,02	0,65	1,24	0,94	0,71	1,22	<0,05*
VLDL, mcmole /l	0,28	0,23	0,33	0,2	0,13	0,25	0,08	0,14	0,24	<0,05*
ASBP(n), mm Hg	116	106	119	119	112	126	121	109	126	<0,05*
GFR ,ml / min	123	117,2	146,02	123,2	110,2	144	116,3	110,7	140,35	<0,05*
% PWLV %	50	33	99	6 63,0	40	100	39	22	71	<0,05*

(*Note:Me- median, LQ- lower quartile, UQ- upper quartile; TG-, triglycerides, VLDL- very low density lipoproteins; ASBP(n)- average systolic blood pressure during the night; GFR- glomerular filtration rate. P- between groups of the genotypes 4a4a, 4b4b.)*

Thus, patients with genotype 4a4a were found to have the highest level of insulin in blood serum and dyslipidemia; besides, patients-carriers of allele a were more frequently diagnosed with signs of myocardial remodeling with involvement of the posterior wall of the left ventricle.

Patients with genotype 4b4b were shown to have the highest indices of average systolic blood pressure during the night. Genotype 4b4a is perhaps an average version between the previous two genotypes.

Thus, it is possible to assume that allele influence and, in particular, the most "unfavorable" genotype 4a4a, is mediated through a number of metabolic disorders, resulting in the progression of atherosclerosis, endothelial dysfunction and myocardial remodeling of the left ventricle.

Interesting data were obtained in the analysis of homocysteine levels in blood serum of patients with different genotype. The study showed the following findings: in patients with genotype 4b4b its level amounted Me = 11.8 [6.9; 17.3] mcmole/l. In children with genotype 4b4a it comprised Me = 12.2 [7.9; 19.3] mcmole/l. In the group of adolescents with genotype 4a4a the level of homocysteine was Me = 2.9 [2.5; 4.6] mcmole/l.

Thereafter, the patients were divided into 4 groups according tocluster 1, 2, 3 or 4, that is by the level of homocysteine in blood serum (Table2).

Table 2.

The level of homocysteine in the blood serum of patients carried to different, clusters mcmole / l.

Cluster	Abs.	%	Mean	Min.	Max.	S.D.	Me	LQ	UQ
1	11	10,9	2,43	1,7	2,9	0,31	2,5	2,3	2,6
2	34	33,7	6,65	3,1	9,8	1,94	6,8	4,9	8,5
3	38	37,6	13,68	10,4	19,3	2,46	13,1	11,5	15,3
4	18	17,8	29,56	21	47,7	8,42	25,9	23,5	37

Note:
Me- median, LQ- lower quartile, UQ- upper quartile.

Thus, the first cluster included 11 adolescents with the lowest content of homocysteine in blood (2.43 ± 0.31 μmol/l). The second cluster (n = 34) comprised patients with the level of homocysteine corresponding to normal indices (6.65 ± 1.94 μmol/l). The third cluster involved 38 patients with the increased level of homocysteine in blood serum (13.68 ± 2.45 μmol/l). The fourth cluster consisted of 18 children with high level of homocysteine (29.56 ± 8.42 μmol/l).

Assessment of the heart remodeling variants according to the level of homocysteine showed that in the group of children with normal and increased homocysteine level the myocardial mass index of the left ventricle (LV) was within the normal range, while the relative thickness of LV wall tended to increase.The patients with the highest level of homocysteine were found to have a significantly reliable enlargement of the relative thickness of LV wall ($p < 0.05$) and an increase in the myocardial mass index of the left ventricle ($p < 0.05$).

The study showed that progression of hyperhomocysteinemia was accompanied by an increase in the incidence of restrictive diastolic LV dysfunction as compared to adolescents with normal blood serum homocysteine level ($p < 0.05$).

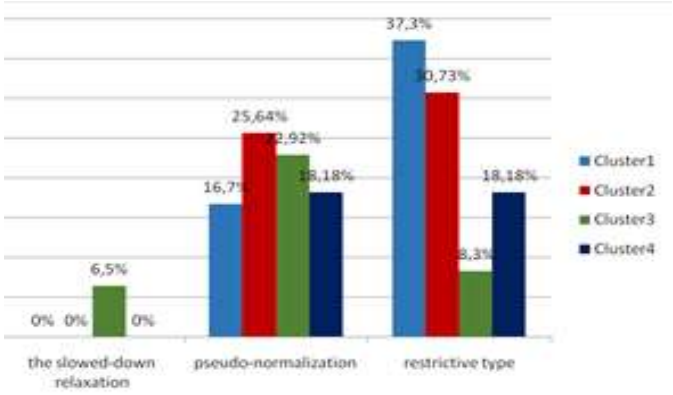

Fig. 1.The frequency of diastolic dysfunction in children with different levels of homocysteine in the serum.

Thus, an increase in blood serum homocysteine level influences the development of LV myocardial remodeling. In normal homocysteine level myocardial geometry is within normal range, whereas an increase in homocysteine level results in the development of concentric remodeling andconcentric hypertrophy of LV myocardium in children with the highest level of homocysteine, which reflects regularities of LV myocardium remodeling.

We investigated blood serum homocysteine level in adoles-

cents with different ENOS genotype. The most obvious differences between the indices of homocysteine in blood serum were observed between patients with 4a4a and 4b4b genotypes.

The nature of these distinctions was clarified by identification of alleles a and b as a sign of "GROUP" sample stratification, as well as by regression analysis in the subgroup of patients with allele a (hereafter - Group A) separately and in the subgroup of patients with allele b (hereafter- Group B).

Thus, the study showed that patients-carriers of allele b with the growth of body mass and progression of abdominal obesity (WM/HM ratio) were more likely to have an increase in the level of homocysteine in blood serum. It promoted progression of hypertension in this cohort of patients. Blood pressure stabilization was rather associated with the involvement of kidneys.The growth of body mass increased the volume of circulating blood and viscosity of blood. Moreover, fatty tissue might release angiotensinogen which resulted in dysfunction of kidneys, responsible for the long-term regulation of blood pressure by changing the activity of RAAS and sodium-volume-dependent systems. Hyperhomocysteinemia itself, as was stated above, promoted myocardial remodeling of the left ventricle.

Thus, patients-carriers of allele b, were found to have a decreased cavity of LV myocardium (concentric remodeling). It was reflected by sphericity index rateswhich as well as the height of the left ventricle decreased in hyperhomocysteinemia progression.

The results for group A regression are shown in Fig. 2. Indices of average diastolic blood pressure during the day and night and average systolic blood pressure during the day and night should be considered the most influential in prognosis of homocysteine level in blood serum for allele a carriers.

Progression of arterial hypertension in this cohort of patients was associated with a change of vascular tone.As was mentioned above, destabilization of vascular wall in genotype 4a4a was influencedby the altered levels of triglycerides, lipoproteins of very low density and hyperinsulinemia.

	regression results for a dependent variable: HOMO (tabl_natali_HOMOx3.sta) R= .64386623 R2= .41456372 Correct. R2= .37348048 F(8.114)=10.091 p<.00000 Standart error of estimate: 8.7864					
	beta	SE,B	B	SE, B	t(114)	p-level
			-38,113	13,491	-2,825	0,006
SADD	-0,564	0,174	-0,629	0,194	-3,248	0,002
DADD	0,706	0,139	1,021	0,201	5,070	0,000
SADN	0,586	0,166	0,651	0,185	3,519	0,001
DADN	-0,562	0,158	-0,748	0,211	-3,544	0,001

Fig. 2.**The summary table of model of linear regression for group A when calculating in statistical environment to the STATISTICA.**
Note: SADD- average systolic blood pressure during the day, DADD - the average diastolic blood pressure during the day, SADN - average systolic blood pressure during the night, DADN- the average diastolic blood pressure during the night, VrSD - variability of systolic blood pressure during the day, VrSN- variability in systolic blood pressure overnight, TZS2 - the thickness of the back wall of the left ventricle in diastole, OTS - relative wall thickness of the left ventricle.

Literature data confirm that nitrogen oxide production is decreased in patients-carriers of allele a [15-17], triggering endothelial dysfunction. In progression of arterial hypertension and hyperhomocysteinemia these patients develop an increase in the thickness of left ventricular posterior wall and relative thickness of left ventricular wall – an integral indicator of myocardial LV remodeling, which is the most typical for concentric hypertrophy of LV myocardium.

Thus, hypothalamic syndrome of puberty is a disorder in children, which develops with arterial hypertension, abdominal type of obesity, disruption of lipid range of blood, hyperinsulinemia. Considering the metabolic essence of HSPas a "prototype" of metabolic syndrome in adults, it is possible to consider that patients with HSP in adulthood are likely to develop cardiovascular impairments. If metabolic disorders typical for HSP have a significant effect on vascular endothelium, in future it will ultimately result in endothelial dysfunction, myocardial LV remodeling, development of diastolic and systolic dysfunction.

4 CONCLUSIONS

1. The increased blood serum homocysteine level (≥10.40 μmol/l) and high homocysteine level (≥21.0 μmol/l) in adolescents is associated with hypothalamic syndrome of puberty with signs of myocardial remodeling and diastolic function of the left ventricle. Progression of hyperhomocysteinemia results in a decrease in indices of LV cavitysphericity.

2. Assessment of endothelial nitric oxide synthase (eNOS) gene polymorphism in adolescents with hypothalamic syndrome of puberty determined genotype 4b/4b in 47% of children, genotype 4b/4a in 43%, genotype 4a/4a in 11% of adolescents. Genotype 4a4a is unfavorable concerning the development of metabolic disorders and is characterized by the highest level of immunoreactive insulin in blood serum (33.2 (16.5; 40.1) uIU/mL), an increased level of triglycerides (1.41 (1.18; 1.64) mmol/l).

3. Adolescents with hypothalamic syndrome of puberty, accompanied by arterial hypertension with different eNOS genotypes, who carry allele b typically develop concentric remodeling ($p < 0.05$), whereascarriers of allele aundergo remodeling of a left ventricular myocardium by the type of concentric hypertrophy.

REFERENCES

1. Kovalenko V.N., Nesukaj E.G., Dolzhenko M.N., Gorbas' I. N. Profilaktika serdechno-sosdistyh zabolevanij: populyacionnaya strategiya I individual'nye programmy. [Prevention of cardiovascular diseases: population strategy and individual programs]. – K.: MORION, 2013, 96.

2. Hypertension without compelling indications: 2013 CHEP recommendations. Hypertension Canada website. – http://www.hypertension.ca/hypertension-without-compelling-indications. AccessedOctober 30, 2013.

3. Urbina E., Alpert B., Flynn J., Hayman L., Harshfield G.A., Jacobson M. et al. American Heart Association Atherosclerosis, Hypertension, and Obesity in Youth Committee. Ambulatory blood pressure monitoring in children and adolescents: recommendations for standard assessment: a scientific statement from the American Heart Association Atherosclerosis, Hypertension, and Obesity in Youth Committee of the council on cardiovascular disease in the young and the council for high blood pressure research // Hypertension 2008. — Vol. 2. —433-451.

4. Mitchenko E.I. .Sovremennyj profil' factora riska serdechno-sosudistyh zabolevanij v gorodskoj populyacii Ukrainy [The modern profile of risk factors of cardiovascular diseases in the urban population of Ukraine]/ E.I. Mitchenko, M.N. Mamedov, T.V. Kolesnikidr. // Mat-ly XIV Nacional'nogo kongresu kardiologiv Ukraïni. – 2013. – 76-83.

5. Korenev N.M. Arterial'naya gipertenziya-podrostkovogo vozrasta: rasprostranennost', mekhanizmy formirovaniya, podhody k lecheniyu [Arterial hypertension of adolescence: prevalence, forming mechanisms, approaches to treatment] / N.M. Korenev, L.F. Bogmat, E.M. Nosova, V.V. Nikonova, Je.L. Ahnazarjanc, I.M. Jakovleva // Ukr. kardiol. zhurn. — 2010. — vol. 1. — 57-64.

6. Moiseienko R. O. Analiz ta tendenciï zahvoryuvanosti dityachogo naselennya Ukraïni./ Moiseenko R. O., Sokolovs'kaJa. I., Kul'chic'kaT. K. , Buhanovs'kaT. M. // Suchasna pediatrija. – no. 3(31). — 2010. – 13-17.

7. Gorbas I.M. Ocinkaposhirenosti ta kontrolyu faktoriv riziku sercevo-sudinih zahvoryuvan' sered naselennya ta likariv [Evaluation of the prevalence of risk factors and control cardiovascular diseases among the population and the physicians] / I.M Gorbas, O.N Barna, VY Sakaloshtainshi // Medytsyna Ukraini. - 2010. – no. 1. - 4-9.

8. Rekomendacii po profilaktike serdechno – sosudistyhzabolevanij v detskom I podrostkovom vozraste [Recommendations about Prevention of cardiovascular diseases in children's and adolescent age] / A.A. Aleksandrov, M.G. Bubnov, O.A.Kisljak, I.V. Leont'evai dr. // Novosti mediciny I farmacii. Kardiologija. — 2012. — no. 439. — 45-77.

9. Li J., Cun Y., Tang W. R. et al. Association of eNOS gene polymorphisms with essential hypertension in the Han population in southwestern China. / J. Li, Y. Cun, W.R. Tang et al. // Genet Mol Res. 2011 Sep 27. Vol. 10(3) .- 222-233.

10. Eckel R.H., Jakicic J.M., Ard J.D. et al. AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association task force on practice guidelines // Circulation. – 2013. – doi: 10.1161/01.cir.0000437740. 48606.d1.

11. Trabetti E. Homocysteine, MTHFR gene polymorphisms, and cardio-cerebrovascular risk. J. Appl. Genet., 2008. —Vol. 49. —267-282.

12. SirenkoJu. M. Arterial'na gipertenziya ta suputnya patologiya. [Arterial hypertension and the accompanying pathology.] — Donec'k: Vidavec' Zaslavs'kij O.Ju., 2010.-384 p.: fig.

13. Bogmat L.F. Izmenenie geometrii levogo zheludochka u detej s pervichnoj arterial'noj gipertenziej [Change of geometry of a left ventricle in children with primary arterial hypertension] / L.F. Bogmat, V.V. Nikonova, I.G. Zaharov // Ukraïns'kij kardiologichnij zhurnal. — 2003. – no.5. —65-69.

14. Pavlova O. S. Tipy remodelirovaniya miokarda-levogo zheludochka pri arterial'noj gipertenzii [Types of remodeling of myocardium of the left ventricle at arterial hypertension] / O.S. Pavlova, T.A. Nechesova // Medicinskaja panorama. – 2012. -78-83.

15. Grøntved A., Andersen L. B., Franks P. W. et al. NOS3 variants, physical activity, and blood pressure in the European Youth Heart Study / A. Grøntved, L.B. Andersen, P.W. Franks et al. // Am J Hypertens. 2011. — Vol. 24(4).— 444-550.

16. Le Couter J., Moritz D. R., Phillips G. L. et al. Angiogenesis-independent endothelial protection of liver: role of VEGF / J. Le Couter, D.R. Moritz, G.L. Phillips et al. // Science 2011. — Vol. 299.— 890 – 893.

17. Chajkovskaja I.V. Endotelial'naya disfunkciya I eyo rol' pri patologicheskih processah [Endothelial dysfunction and its role in pathological process I.V.Chajkovskaja, O.A. Semenova] // Univ. klinika: Naukovo-praktichnij zhurnal. — 2011. — no. 7(2). —210-213.

РЕЗЮМЕ

Гончарь М.О., Коновалова Н.В., Муратов Г.Р.

МЕХАНІЗМИ РЕМОДЕЛЮВАННЯ МІОКАРДУ У ПІДЛІТКІВ З ГІПОТАЛАМІЧНИМ СИНДРОМОМ ПУБЕРТАТНОГО ПЕРІОДУ ТА АРТЕРІАЛЬНОЮ ГІПЕРТЕНЗІЄЮ

Харківський національний медичний університет

Авторами вивчені моделі ремоделювання міокарда лівого шлуночка у підлітків із гіпоталамічним синдромом пубертатного періоду та артеріальною гіпертензією в залежності від поліморфізма гена ендотеліальної синтази оксиду азоту в інтроні 4 (4b,4a) та рівня гомоцистеїну сироватки крові.

Ключові слова: поліморфізм гена, ендотеліальна NO-синтаза, гомоцистеїн, підлітки, ремоделювання міокарда, артеріальна гіпертензія.

РЕЗЮМЕ

Гончарь М.О., Коновалова Н.В., Муратов Г.Р.

МЕХАНИЗМЫ РЕМОДЕЛИРОВАНИЯ МИОКАРДА У ПОДРОСТКОВ С ГИПОТАЛАМИЧЕСКИМ СИНДРОМОМ ПУБЕРТАТНОГО ПЕРИОДА И АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИЕЙ

Харьковский национальный медицинский университет

Авторами изучены модели ремоделирования миокарда левого желудочка у подростков с гипоталамическим синдромом пубертатного периода и артериальной гипертензией в зависимости от полиморфизма гена эндотелиальной синтазы оксида азота в интроне 4 (4b,4a) и уровня гомоцистеина сыворотки крови.

Ключевые слова: полиморфизм гена, эндотелиальная NO-синтаза, гомоцистеин, подростки, ремоделирование миокарда, артериальная гипертензия.

Received: 23-Feb. – 2016
Accepted: 25-Mar. - 2016

PEDIATRICS

G.S. Senatorova, L.N. Chernenko, I.V. Korneyko

SPIRAL COMPUTED TOMOGRAPHY IN DIAGNOSIS OF BRONCHOPULMONARY DYSPLASIA

Kharkiv National Medical University, Ukraine

Abstract: Bronchopulmonary dysplasia is one of the pressing challenges in pediatrics, which significance goes beyond the field of neonatology and is regarded as a chronic obstructive disease of young children. The article presents an assessment of typical chest radiographic findings detected by spiral computed tomography according to the form of the disease.

KeyWords: Bronchopulmonary dysplasia, spiral computed tomography, chest cavity, children.

INTRODUCTION

A concept of natural disease development has been formed for a number of pathological conditions, that is disease course from the onset to regress or control, which is understood as the programs aimed at reducing the incidence or prevalence or elimination of these diseases. Bronchopulmonary dysplasia in this regard is not an exception [1]. However, despite the scientific process in the study of etiological factors, pathogenesis and clinical presentation of bronchopulmonary dysplasia, the desired level of control over the disease has not been achieved [1, 2].

The diagnosis of bronchopulmonary dysplasia (BPD) is clinical radiological. According to the literature, radiological methods are leading not only in the diagnosis of BPD, but in recognition of its consequences and complications [3, 4, 6]. Radiographic study is used for follow-up monitoring of the disease development in the lungs. W. H. Northway described 4 radiographic successive stages of BPD. However, not all children demonstrate stages in BPD formation.

• *Corresponding Author:*

***Larysa Chernenko**, MD, PhD, Assistant of Professor, Department of Pediatrics 1 and Neonatology, Kharkiv National Medical University, Ukraine. E-mail: chernenko.larysa@gmail.com*

Development of BPD is possible with minimal radiographic changes inherent to the new form of BPD and do not fit those described by W. N. Northway. This requires further study of this issue. The methods of X-ray diagnosis visualize macrostructure and anatomical topographic features of the respiratory organs [6]. According to many authors, the combined analysis of these data and the findings of clinical and laboratory investigation can improve sensitivity and specificity of each of them as well as allow to switch from probable to nosological diagnosis. Many researchers consider that doing plain chest X-ray the doctors face the problem of projection and summary distortion of the pulmonary picture. And it is not always regarded as morphological changes characteristic of bronchopulmonary dysplasia [6, 7]. This is due to the fact that traditional radiography is insufficiently informative because due to superposition and subtraction the X-ray images poorly resemble a morphological substrate, which sometimes complicates clinical and radiological diagnosis of BPD [6]. Therefore, the search for more informative and highly sensitive imaging methods was justified. Introduction of spiral computed tomography (SCT) into the diagnosis of chronic lung diseases in children, which is due to its high sensitivity has the ability to detect the details inaccessible by the traditional X-ray examination, led to a real revolution in this area. According to many authors, the advantages of CT include the capability to explore subtle signs of parenchy-

mal changes in a separate section of the lungs, spatial location of trachea, vessels, bronchial tree [6, 7]. Thus, radiographic diagnosis is the leading instrument in identification of bronchopulmonary dysplasia in children. However, the data of Ukrainian and foreign literature are controversial and the problem has not been investigated in detail, which dictates the need for further improvement and refinement of radiological semiotics of bronchopulmonary dysplasia, according to the form of the disease, determination of prognostic signs of respiratory and cardiovascular complications in children with bronchopulmonary dysplasia.

2 PURPOSES, SUBJECTS AND METHODS:

2.1 Purpose

To improve diagnosis of various forms of bronchopulmonary dysplasia by identification of specific radiological changes using spiral computed tomography of the chest.

2.2 Subjects

The study was conducted at the Department of Pediatrics No. 1 and Neonatology of KhNMU (Head of Department – Doctor of Medical Science, Professor H.S.Senatorova) at Regional Centre for Diagnosis and Treatment of Bronchopulmonary Dysplasia in Children (Head of the Center – Candidate of Medical Science, O.L.Logvinova) of Kharkiv Regional Children Clinical Hospital (Head Doctor – Candidate of Medical Science, Associate Professor H.R.Muratov).

The study group included 71 children aged 1 month - 3 years, of them 35 (49.3%) were diagnosed with classical form of BPD (group 1), 19 (26.8%) a new form of BPD (group 2), 17 (23.9%) full-term BPD (group 3).

2.3 Methods

The diagnosis of bronchopulmonary dysplasia was made according to the International Classification of Diseases, revision 10 (P 27.0). Severity criteria were determined by clinical forms of bronchopulmonary diseases in children of Russian Respiratory Society (2009) [8]. Radiographic criteria were evaluated on the 28th day of life by spiral computed tomography of the chest in the phase of physiological or pharmacological sleep. The study was performed in accordance with the ethical principles of medical research involving human subjects that have been approved by Helsinki Declaration. Statistical analysis of the findings was performed using statistical software package Statistica 7.0. Median (Me) and interquartile scope (Lq - bottom quartile; Uq - top quartile) were determined for samples with distribution that did not comply with Gaussian law. Nonparametric U-Mann-Whitney test (MW) was used to compare two samples. To compare the values, which were characterized by opposing more than 2 points, Kruskal-Wallis analysis of variance was used, the differences were considered probable with Bonferroni adjustment (at $p^{\wedge} = p / k$, where k is the number of paired comparisons). Fisher's criterion (F) was used to compare two variances. The method of angular transformation of F-test assessment was used to contrast sample particles. The findings were considered statistically significant at values of $p < 0.05$.

2.4 Conflict of interests

There is no conflict of interests.

3 RESULTS AND DISCUSSION

Group age patterns in children with BPD coincided with the relevant trends in general, namely, demonstrated statistically significant predominance of patients of the first year of life among the total number of patients (Group 1 – 81.4 ± 6.0%; Group 2 – 77.4 ± 9.1%; group 3 – 61.1 ± 7.5%, respectively). By sexual dimorphism the majority of children with various forms of bronchopulmonary dysplasia were boys.

Multiple comparison using Kruskal-Wallis analysis of H criterion for gestation term and birth weight high (Table 1) allows to suggest that statistical characteristics of different groups of children with bronchopulmonary dysplasia were quite different, and the level of these values depended on a particular group.

Table 1

Statistical characteristics of the parameters of gestation period and body weight in children with bronchopulmonary dysplasia

Parameter	Statistical value	Groups		
		Group 1	Group 2	Group 3
Gestation period	Me	32	27	38
	(Lq; Uq)	(28; 34)	(26; 30)	(38; 39)
KW ANOVA by Ranks: H=44.9, p=0.0000; MW U Test: p_{1-2}=0.0007;p_{1-3}=0.0000; p_{2-3}=0.0000;				
Body weight at birth	Me	1700	1105	2835
	(Lq; Uq)	(1100; 2390)	(800; 1450)	(2480; 3500)
KW ANOVA by Ranks: H=32.5, p=0.0000; MW U Test: p_{1-2}=0.005; p_{1-3}=0.00001; p_{2-3}=0.0000				

In pairwise comparison with nonparametric Mann-Whitney (MW) method, p <0.017 was taken as the level of statistical significance of differences between the groups, according to Bonferroni correction. The presence of possible differences in children with bronchopulmonary dysplasia was determined only by gestation period and birth weight, reflecting the immaturity of all organs and, first of all, bronchopulmonary system. The assessment of correlations between groups 1 and 2 demonstrated that the level of correlation between the gestation period and the duration of mechanical ventilation was significantly higher (p = 0.0199) than between the period of gestation and birth weight (p = 0.2024) and between birth weight and duration of mechanical ventilation (p = 0.8001). Mature children with bronchopulmonary dysplasia were not found to have possible links between the period of gestation, birth weight, duration of mechanical ventilation and oxygen dependence (all p> 0.05). Primarily, this is due to the fact that the children from group 3 were full-term and failure of spontaneous unassisted respiration was not associated with the development of respiratory disorders inherent to premature babies, but the presence of comorbidities, which severity necessitated artificial ventilation (CNS congenital lesions, abnormal development, and surgery).

Assessment of specific radiological changes on plain chest film in bronchopulmonary dysplasia showed that fibrosis and interstitial changes in Group 1 were diagnosed only in every eighth child, Group 2 - one in four, and group 3 - every second child (Table 2).

Table 2

The frequency of radiographic changes of the chest in children with bronchopulmonary dysplasia

Sign	Group 1 n=35	Group 2 n=7	Group 3 n=12
	$p\%\pm s_{p\%}$	$p\%\pm s_{p\%}$	$p\%\pm s_{p\%}$
Signs of hyperinflation: -increased lung markings	74.3±7.4	71.4±18.4	83.3±11.2
-enriched lung markings	100.0±0.02	71.4±18.4	83.3±11.2
-lengthening of the lung fields	57.1±8.4	42.9±20.2	58.3±14.8
-indistinct lung fields	48.6±8.5	14.3±14.3	66.7±14.2
-increased transparency of the lung tissue	71.4±7.7	57.1±20.2	58.3±14.8
Fibrosis or interstitial changes	22.9±7.2	57.1±20.2	16.7±11.2

That is, changes in plain X-ray investigation cannot always be interpreted as morphological features of bronchopulmonary dysplasia. According to the literature, pathomorphological signs of bronchopulmonary dysplasia at postmortem examination develop on the 6th day of the infant's life [9]. It is not surprising that changes on CT scans of the chest were detected in all the examined children with various forms of BPD. All children with bronchopulmonary dysplasia, regardless of the particular form, were found to have fibrotic changes in the lung parenchyma, adhesions, pleural thickening and emphysema (Table 3). However, evaluation of CT changes in the lungs in children with various forms of BPD demonstrated some peculiarities. In Group 1 children mosaic marking of lung tissue was observed much more frequently than in Group 2 (F1-2=4.4; p<0.05), and areas of consolidation occurred significantly more often than in Group 3 (F1-3=4.05; p <0.05). In Group 2 relative number of children with pleural thickening and pneomocele was significantly higher than in Group 3 (F2-3=4.11; p <0.05 and F2-3= 6.0; p <0.05, respectively).

Table 3

The frequency of radiographic changes of the chest in children with bronchopulmonary dysplasia

Sign	Group 1 n=35	Group 2 n=7	Group 3 n=12
	$p\%\pm s_{p\%}$	$p\%\pm s_{p\%}$	$p\%\pm s_{p\%}$
Thickening of interlobular septum	42.9±8.4	26.3±10.3	31.3±11.9
Thickening of intralobular interstitial tissue	40.0±8.4	36.8±11.3	68.8±11.9
Striped parenchymal bands	40.0±8.4	42.1±11.6	18.8±10.1
Pleuropulmonary adhesions	17.1±6.4	26.3±10.3	12.5±8.5
Pleurophrenic adhesions	20.0±6.8	10.5±7.2	12.5±8.5
Pneumocele	11.4±5.4	31.6±10.9	6.3±6.3
Frozen glass sign	34.3±8.1	47.4±11.7	25.0±11.1
Fibrotic parenchymal scars	34.3±8.1	31.6±10.9	50.0±12.9
Increase and deformation of the lung markings pattern	34.3±8.1	21.1±9.6	37.5±12.5
Net picture	14.3±6.0	10.5±7.2	43.8±12.8
Thymomegaly	5.7±3.9	10.5±7.2	0.0±0.06
Reduced lung airiness	14.3±6.0	5.3±5.3	12.5±8.5
Areas of lung tissue consolidation	8.6±4.8	5.3±5.3	0.0±0.06
Mosaic of lung marking	8.6±4.8	0.0±0.05	6.3±6.3
Pleural thickening	2.9±2.9	15.8±8.5	0.0±0.06

Every second child of Group 3 had interlobular interstitial thickening (F3 = 5.1; $p < 0.05$), and the proportion of children who were diagnosed with net picture in the lung tissue was significantly greater in contrast to the children of Groups 1 and 2 (F1-3= 5.1, $p < 0.05$; F F2-3= 5.5, $p < 0.05$).

Thus, assessment of frequency of SCT changes in children with various forms of bronchopulmonary dysplasia allowed to suggest that radiographic methods, especially spiral computed tomography of the chest, are a "gold standard" in the diagnosis, follow-up monitoring of the disease development in the lungs and evaluation of the response to treatment

4 CONCLUSIONS

1. Spiral computed tomography of the chest can detect minimal changes of the lung parenchyma and thus, plays an important role in the diagnosis of bronchopulmonary dysplasia in children.
2. Children with classical form of bronchopulmonary dysplasia much more frequently develop diffuse striped fibrosis secondary to significant hyperinflation, reflecting more severe lesions in the lung tissue.
3. Interstitial changes with minimal signs of fibrosis are more likely to occur in patients with a new form of bronchopulmonary dysplasia, as evidenced by the more frequent incidence of pneumocele.
4. Full-term children with bronchopulmonary dysplasia were found to have signs of thickening and intralobular interstitial net picture with marked fibrotic changes of the lung tissue.

REFERENCES

1. Ovsiannikov D., Kuz'menko L, Degtyareva E. (2007) Techenie bronholegochnoj displazii u detej grudnogo I rannego vozrasta [The course of bronchopulmonary dysplasia in infants and early-age children]. Pediatria, no 86 (4), pp.35-42.
2. Senatorova A., Logvinova O., Muratov G., Zolotuhina G., Chernenko L. (2010) Bronholegochnayadisplaziya u detej. Sovremennyj vzglyad na problem diagnostiki I lecheniya [Bronchopulmonary dysplasia in children. Modern approach to the problem of diagnosis and treatment]. Sovremennaya pediatriya, no 1 (29), pp.105-112.
3. Kozarezov S. (2007) Sovremennyepredstavleniya o bronholegochnojdisplazii u detej (chast' 2) [Modern concepts of bronchopulmonary dysplasia in children (Part 2)]. Medicinskij zhurnal, no 4, pp.15-24.
4. Starevskaya S. (2001) Bronholegochnaya displaziya u detej (factory riska formirovaniya, kliniko-rentgenologicheskie osobennosti razlichnoj stepeni tyazhesti zabolevaniya) [Bronchopulmonary dysplasia in children (risk factors of formation, clinical and radiological

features of disease severity)]. Avtoref.diss.…kand.med.nauk, SPb.

5. Shishko G. (2006) Sovremennye podhody k rannej diagnostike I lecheniyu bronholegochnoj displazii [Modern approaches to the early diagnosis and treatment of bronchopulmonary dysplasia]. Uchebno-metodicheskoe posobie dlya vrachej, Minsk, pp. 31.

6. Cpuzyak M., Shapovalova V., Voron'zhevI.,KramnijI. (2008) Bronholegeneva displaziya (ponyattya, terminologiya, promenevadiagnostika [Bronchopulmonary dysplasia (concepts, terminology, radiodiagnosis)]. Ukraïns'kij Radiologichnij zhurnal, no 5, pp.386-392.

7. Tyurin I. (1999) Metody rentgenologicheskoj diagnostiki [Methods of X-ray diagnosis]. Medicinskaya vizualizaciya, no 3, pp.36-44.

8. Geppe N., Rozinova N., Volkov I., Mizernickij Yu. (2009) Rabochaya klassifikaciya osnovnyh klinicheskih form bronholegochnyh zabolevanij u detej [Working classification of the main clinical forms of bronchopulmonary diseases in children]. Moskovskij NII pediatriiidetskoj hirurgii, Prakticheskaya medicina, pp. 46.

9. Dobryak T., Perevoshhikova N. (2008) Sovremennye aspekty bronholegochnojdisplazii [Modern aspects of bronchopulmonary dysplasia]. Mat' I Ditya v Kuzbasse, no 3 (34), pp.3-6.

РЕЗЮМЕ

Сенаторова Г.С., Черненко Л.М., Корнейко І.І.

ЗНАЧЕННЯ СПІРАЛЬНОЇ КОМП'ЮТЕРНОЇ ТОМОГРАФІЇ В ДІАГНОСТИЦІ БРОНХОЛЕГЕНЕВОЇ ДИСПЛАЗІЇ

Харківський національний медичний університет

Бронхолегенева дисплазія – одна із актуальних проблем педіатрії, значення якої виходить за межі неонатології і розглядається як хронічне обструктивне захворювання дітей раннього віку. У статті наведений аналіз характерних рентгенологічних змін методом спіральної комп'ютерної томографії органів грудної порожнини в залежності від форми захворювання.

Ключові слова: бронхолегенева дисплазія, спіральна комп'ютерна томографія, органигрудноїпорожнини, діти.

РЕЗЮМЕ

Сенаторова А.С., Черненко Л.Н., Корнейко И.И.

ЗНАЧЕНИЕ СПИРАЛЬНОЙ КОМПЪЮТЕРНОЙ ТОМОГРАФИИ В ДИАГНОСТИКЕ БРОНХОЛЕГОЧНОЙ ДИСПЛАЗИИ

Харьковский национальный медицинский университет

Бронхолегочная дисплазия – одна из актуальных проблем педиатрии, значение которой выходит за пределы неонатологии и рассматривается как хроническое обструктивное заболевание детей раннего возраста. В статье приведен анализ характерных рентгенологических изменений методом спиральной компьютерной томографии органов грудной полости в зависимости от формы заболевания.

Ключевые слова: бронхолегочная дисплазия, спиральная компьютерная томография, органы грудной полости, дети.

Received: 20-Feb. – 2016
Accepted: 24-Mar. - 2016

PEDIATRICS

G.S. Senatorova, M.O. Gonchar, O.L. Logvinova, M.I. Strelkova

DIGEORDGE SYNDROME

(Case)

Kharkiv National Medical University, Ukraine

Abstract: The article presents a clinical report on DiGeorge syndrome. The study involved the assessment of disease presentation, diagnosis, inpatient management and recommendations for the follow-up treatment at home.

Key Words: DiGeorge syndrome, primary immune deficiency, children, treatment.

———————————❖———————————

Patient T., a 1.5-months-old boy, was admitted to the Intensive Care Unit in a severe condition due to cardiorespiratory failure and absence of spontaneous respiration, and was intubated with an oro-tracheal tube.

Assessment of the past and disease history showed that the child was from the 4th pregnancy, 2-nd spontaneous vaginal delivery at 38 weeks of gestation. During this pregnancy his mother experienced a threatened miscarriage at 24 weeks, an acute respiratory viral infection at 26 weeks, and asymptomatic bacteriuria from the 34-th week. Ultrasonography did not reveal any abnormalities at 11-12 weeks of gestation and anything abnormal at 25-26 weeks; echoscopic examination of fetus at the 34-th week detected signs of multiple congenital malformations (congenital heart disease, dilation of the right compartment of the heart and pulmonary artery, enlargement of the cavity of septum pellucidum to 9 mm). The findings were also indicative of hypoplasia or agenesis of the corpus collosum, hypoplasia of the vermis cerebelli, varus of the right foot, hydrocele, single umbilical artery, placental hypoplasia and polyhydramnios.

• ***Corresponding Author:***
***Olga Logvinova**, MD, PhD, Associate Professor, Department of Pediatrics 1 and Neonatology, Kharkiv National Medical University, Ukraine. E-mail: ologvinova76@mail.ru*

Family history was aggravated by multifactorial diseases: the child's mother (34 years old) had chronic pyelonephritis in remission, varicose veins of the legs. His father (36 years old) was healthy. His brother (7 years old) and sister (9 years old) were healthy.

At birth the child weighed 3150 g, his height was 53 cm, head circumference — 34 cm, chest circumference — 34 cm, Apgar score: 1 min — 7 points (2-2-1-1-1), 5 min - 8 points (2-2-1-1-2).

On the second day after the birth he was referred to a surgical correction of congenital heart defect (expansion of the aortic arch, aortic coarctation, ligation of patent ductus arteriosus) at Cardiosurgery Department. Eight days after surgical intervention he was transferred to Perinatal Center, where he was rendered respiratory support due to absence of spontaneous respiration.

He was diagnosed with hypoplastic left-heart syndrome, moderate hypoplasia of the left ventricle and aortic valve, hypoplasia of the aortic arch, patent ductus arteriosus, secondary atrial septal defect. The patient was examined by a geneticist, DiGeorge syndrome was suspected.

He was treated using open resuscitation system Aveo with respiratory support, received nutrition through a feeding tube, and was administered furosemide, captopril, verospiron, antibacterial, fungicide and immunomodulatory therapy as well as feet bandaging.

The child's condition remained severe due to evident signs of cardiorespiratory failure and absence of spontaneous respiration. He was referred to further follow-up treatment in a multi-field hospital.

On admission his consciousness was clear, his skin was pale; widespread venous network, underdeveloped subcutaneous fat layer, signs of connective-tissue dysplasia (hypermobility of the joints, hyperextensibility of the skin, varusof feet), rightsided hydrocele were detected. Visible mucous membranes were pink. Body temperature was within normal range. His heart rate was 160/min, BP — 80/60 mmHg, SpO_2 — 99%,body mass -3950 g,height -54.8 cm; head circumference — 36.5 cm, chest circumference — 35.3 cm.

The patient was intubated with an oro-tracheal tube, his respiration was harsh, and wheezing was not heard. Heart tones were rhythmic. The abdomen was soft, deeply palpable in all areas. The liver was enlarged to 3 cm below the costal margin, the spleen is +2 cm below the costal margin. Bowel movements were normal.

On admission the following diagnosis was made: DiGeorge syndrome, multiple congential malformations, congenital heart defect: hypoplastic left heart, hypoplasia of the aortic arch, aortic coarctation, patent ductus arteriosus. After surgical intervention the patient had secondary atrial septal defect, cardiomegaly, aplasia of the thymus, congenital malformation of the urinary system: grade IV hydronephrosison the leftside, congenital right clubfoot, bilateral pneumonia with confluent foci. The patient was referred to laboratory and instrumental studies with consultations by the specialists of related fields.

-Blood count:

The day in the station /№	Hb	RBC	Reticuocytes, %	Plateletes	WBC	basophils	eosinophils	granulocytes	lymphocytes	monocytes
2nd/1	79	2,8	0,87	146	4,6		1	55	36	8
4th/2	93	3,2	0,87	139	6,7		2	70	17	10
9th/3	74	2,6	0,5		4,3		1	60	31	8
13th/4	125	4,1	0,9	213	8,6		1	65	25	9
17th/5	97	3,3	0,89	165	8,2	1	1	44	52	2
13th/6	111	3,7	2,0	274	5,8		1	72	23	1

Liver function tests - ALT (N 0.14) - 0.07 mkkat/l; AST (N 0.14) - 0,083mkat/l; B-lipoproteins - 34; Cholesterol - 2,49 mmol/l; thymol test - 1.0; alkaline phosphatase - 5600 U/l; total bilirubin - 9,9 mmol/l; direct - 3.3 mmol/l; indirect - 6.6 mol/l.

- Clinical urine analysis:

The day in the station /№	Quantity	Color	CLA	SG	Protein	RBC	WBC
2nd/1	10,0	Yellow	Bland	-	None	1-2	1-3
4th/2	14,0	Yellow	Bland	-	None	1-2	1-3
9th/3	10,0	Yellow	Bland	-	None	1-2	1-3
13th/4	7,0	Yellow	Bland	-	None	1-2	1-2
23th /5	50	Light yellow	Bland	1,006	None	Changed	2-4

- Sputum analysis:

The day in the station /№	Color	Cul-ture	WBC	RBC	Epith eliu m.	Other	MBT
11th/1	White	Muco-puru-lent	10-15	1-3	Squa mose 2-4	None	Abs.
15th/2 (broncho-scopy)	Light white	Puru-lent	40-50	2-4	Squa mose 1-2	Fungus a little	Abs.

-Immunogram:

The day in the station /№	6th day/1	Norm
Leukocytes 10^9/l	10,1	10,3-11
Lymphocytes,%	14	52-69
absolutenumber, 10^9/l	1,42	5,4-7,59
T-Lymphocytes(CD_3),%	63	58-67
absolutenumber, 10^9/l	0,89	1,7-3,6
BLymphocytes. (CD_{22}),%	22	19-31
absolutenumber, 10^9/л	0,31	0,5-1,5
CD_4	45	38-50
CD_8	19	18-25
CD_4/ CD_8	2,37	1,5-2,9
CD_{16}	13	8-15
IgA,g/l	0,57	0,21±0,13
IgM,g/l	0,47	0,30±0,11
IgG,g/l	9,9	4,30±1,19
% neutrophils phagocytose	53	40-90
Phagocytes,number.	1,43	1-2
HCT-test	31	8-12
Compliment CH_{50}	42	40-80

- Bacteriological inoculation from the mouth:

K. Pneumonia 10^7, P. Aeroginosa-10^3;

K. Pneumonia 10^6, P. Aeroginosa- 10^6;

K. Pneumonia 10^4, P. Aeroginosa- 10^7;

K. Pneumonia 10^5, P. Aeroginosa - 10^7.

- Chest X-ray in the first day – bilateral upper lobe pneumonia with confluent foci. On the 13-th day – negative dynamics in the form of atelectasis of the upper lobe of the right lung (the development of segmentary pneumonia is possible). On the 17th day positive dynamics in the form of recovery of pneumatization of lung fields.

- Echocardiography:

The day in the station/№	1st day/1	8th day2	14th day/3	21st day /4	25th day/
EDD	14,3	17,7	15,5	17,4	15,7
ESD	6,1	8,8	19,2		6,8
Vd	5,3	9,3	5,7		6,8
Vc	0,5	1,5	1,6		0,7
Strokevolume	4,8	7,8	4,0		6,1
EF	90	84	71	89	88
Δ D	0,58	0,50	0,37		0,56
dLA			21,0x15,0	12,0	17,9
dRV	18,6	15,0	20,5	19,9	17,9
dRA			19,0x17,0	17,1	
ΔP AV	9,4	13,4	12,4	11,5	10,0
ΔP desc.Ao	15,4	28,5	19,8	14,7	15,1
ΔPAoV	9,3	10,9	3,8		3,9
ΔP MV	6,5	6,5	3,9		4,01
ΔP TV		4,5	5,1	5,7	5,1
Mediumpressure in PA		47,0	34	31	34
dofaorta	7,5				
daorticarch	15,5				
d abdominal. Ao	5,8				
Bloodflowintheabdominalaorta	pulsatile, c V max^2 55 см/с	Pulsatile, c V max^2 58,5 см/с	pulsatile		pulsatile
Regurgitation		I grade		I grade	I grade

- Ultrasonography of kidneys and bladder: hydronephrosis of the left kidney.

- Ultrasonography: the thymus is not visualized.

- Electrocardiography (ECG) on the 2-nd day showed the signs of severe sinus tachycardia, delayed atrioventricular conduction, incomplete right bundle branchblock, hypertrophy of the right atrium and right ventricle, repolarization disturbances. The follow-up findings indicated intensified overload of the left atrium and right ventricle as well as repolarization disturbances.

- Neurosonography: asymmetry of the lateral ventricles, cranial hypertension.

-Immunological findings: thymicaplasia, impaired cellular immunocompetence, DiGeorge syndrome.The patient was referred to chest CT to exclude malformations of the bronchopulmonary system (polycystic hypoplasia) and Wilson-Mikity syndrome.

- Hematological findings: anemia, thrombocytopenia, leukopenia requiring to exclude the development of secondary aplastic anemia. Myelography is necessary if changes in blood persist.

- Neurological findings: hypoxic-ischemic disorder of the central nervous system (of perinatal somatogenic origin), asthenic syndrome.

The patient was treated using open resuscitation system Aveo with respiratory support. He received nutrition through a feeding tube and was administered furosemide, diazepam, armadin, prednisolone, as well as antibacterial and antifungal therapy. Inhalation therapy involved pulmicort, ventolin, lasolvan; per oral thrapy - pyobacteriophagum, sildenafil, captopril, hydrochlorothiazide, verospiron, BioGaia, Laferobionum, Tobrex, caffeine-sodium benzoate (when transferring from respiratory support), pancreatine. The feet were bandaged to correct congenital clubfoot.

From the 7th day of hospital stay the patient developed low-grade fever (37.3-37.5°C), and from the 10th daypyretic fever (38.3-38.5°C) with occasional attacks of bronchospasm. He was diagnosed with secondary bilateral pneumonia with confluent foci andtype IIrespiratory failure. On the 13th day of hospital stay he was found to have negative course of pneumonic process (atelectasis of the upper lobe of the right lung and progression of segmental pneumonia). Positive course was reached by the 15th day.

By day 22, the child restored spontaneous breathing, by the 24th day he was transferred to natural feeding (mother's breast on demand).

Final diagnosis:

Multiple congenital malformations: congenital heart disease (hypoplasia of the aortic arch, patent ductus arteriosus (state after correction: expansion of the aortic arch, excision of aortic coarctation, ligation of patent ductus arteriosus), secondary atrial septal defect,circulatory failure 2A). Congenital defect of the urinary system (polycys-

tic left kidney disease, hydrocele testis). DiGeorge syndrome (thymicaplasia, impaired cellular immunocompetence). Secondary chronic obstructive pyelonephritis in remission. Interstitial lung disease (fibrosis), high pulmonary hypertension, type II respiratory failure. Grade II right-sided pneumonia. Congenital right clubfoot. Tonic and kinetic disorders resulting from hypoxic-ischemic impairment of the central nervous system. Grade II hypotrophy. Anemia, thrombocytopenia.

On the 27-th day of hospital stay the patient was discharge in a stable condition withrecommendations: nutritional care according to age; Eroton 7.5 mg 3 times per day; hydrochlorothiazide 4 mg x 2 times a day; verospiron 7.5 mg x 2 times a day; Captopril 1.4 mg x 2 times a day; Pulmicort 125 μg x 2 times a day for a month and follow-up examination in the hospital.

Literary reference

Di George's syndrome is a primary immunodeficiency characterized by aplasia or hypoplasia of the thymus and parathyroid glands, congenital heart defects, facial malformations. Moreover, the disease may be accompanied by other developmental anomalies (anomalies of the skeleton, kidneys, nervous system, eye disorders).

In absent or, which occurs more often, underdeveloped thymus T-lymphocytes do not develop properly. Therefore, the immune system cannot fully perform its protective function. However, absolute Di George's syndrome with severe abnormalities of the immune system is extremely rare. Due to the variety of symptoms, these patients can be examined by physicians of different specialties [1].

Symptoms. The incidence of this condition is similar both in male and femalepatients.

The standard history includes frequent viral, fungal and bacterial infections, poorly amenable to standard therapy.

Congenital heart defects (to the extent of tetralogy of Fallot-right ventricular outflow obstruction, high ventricular septal defect, aortic dextraposition, right ventricular hypertrophy). Convulsions (due to malfunctioning of the parathyroid glands) [2]. Abnormalities of the facial bones: microcephaly (decreased size of the skull bones); hypertelorism (wide-set eyes); small, deformed, low-set ears; epicanthus (vertical folds of skin of crescent shape covering the inner canthus); cleft lip and palate; "Gothic palate" (high palate); micrognathia (underdevelopment of the jaw bones); strabismus (squint); palpebral fissure (eye shape, in which the outer corners of the eyeballs are lowered).

Abnormalities of the larynx, pharynx, trachea, inner ear, esophagus (stenosis, shortening) [3].

Abnormalities of the central nervous system: cortical atrophy (loss of many motor and sensory functions), hypoplasia (discoordination) of the cerebellum.

Abnormalities of the gastrointestinal tract: atresia of the anus, anal fistula.

Abnormalities of the eyes: coloboma (a defect of one of the components of the eyeball (iris, lens, etc.), in which some components are missing), retinal vascular anomaly (as a result, retinal dystrophy).

Maldevelopment of the kidneys: hydronephrosis, renal atrophy, reflux.

Abnormalities of the teeth: delayed eruption, enamel hypoplasia, dental caries.

Abnormalities of the skeleton: polydactyly, absence of nails, spontaneous bone fractures.

Mental retardation and motor delay [4].

Causes. DiGeorge syndrome is caused by a deletion of the 22nd chromosome. Possible risk factors for the development of deletions are maternal diabetes, alcohol consumption during pregnancy, viral diseases in the first trimester of pregnancy.

There is evidence that damaged 22nd chromosome can be inherited in an autosomal dominant manner, that is, in humans the disease is transmitted from one of the parents [5].

Diagnostics. Assessment of medical history and presentation–mental retardation (according to parents); caries; fractures; heart problems; often recurrent bacterial, viral and fungal diseases unresponsive to treatment.

Study of life history - growth and development retardation; congenital heart defects, strabismus,recurrent bacterial, viral and fungal infections.

On examination: microcephaly, hypertelorism (wide-set)eyes, small, deformed and low-set ears, epicanthus (vertical folds of crescent-shaped skin, covering the inner canthus), cleft lip and palate, "Gothic palate", micrognathia (underdevelopment of the jaw bones), strabismus (squint), palpebral fissure (eye shape, in which the outer corners of the eyeballs are lowered). Specific sounds typical for congenital malformations of the cardiovascular system on auscultation.

Immune status is presented by low T lymphocytes and low serum immunoglobulinscan be detected as well.

Common blood count - lymphopenia.

Biochemical blood assay - decrease in the level of calcium, hypocalcemia (the assay is repeated several times to determine the persistence of this condition).

Ultrasonography of the parathyroid glands and thymus reveals their absence or dystrophy.

Echocardiography of the heart identifies defects of the cardiovascular system.

Fluorescent DNA hybridization detects a deletion of the 22nd chromosome typical forDiGeorge syndrome [6].

Treatment of the Di George's syndrome. Antibiotics are prescribed inbacterial infections,antivirals in viral infections andantifungal drugs in fungal infections. Replacement therapy with intravenous immunoglobulins derived from plasma of healthy donorsin reduced level of immunoglobulins. Calcium supplementation is prescribed in order to increase its level.

Surgical treatment implies correction of congenital malformations of the cardiovascular system.

Transplantation of fetal thymus without prior surgical correction of congenital heart disease is considered to be inefficient, only carried out inabsolute Di George syndrome (in severe immunological disorders, such as severe immunodeficiency).

Complications and consequences. Severe mental retardation.

Development of autoimmune diseases (these diseases are characterized by an aggression of the immune system against its own organism: the immune system takes over its foreign cells and attacks them). Development of neoplastic disease at early age.

Lethal outcome is possible due toinfectious complications or malformations of the cardiovascular system not compatible with life, endocrine disorders (dysfunction of the parathyroid glands).

Prognosis usually depends on the severity of cardiac and endocrine defects, absolute syndrome - on immunological findings - absence of T-lymphocytes, reduced production of antibodies-immunoglobulins**.**

Prevention. Patients with partial immune disorders can be administered prophylactic antibiotic and antifungal therapy.

It is necessary to eliminate the use of alcohol during pregnancy.

Prior to pregnancy, the mother should necessarilybe administered appropriate anti-viral vaccines (e.g., measles and rubella virus).

If routine screening(ultrasound examination of the fetus and pelvic organs at the 11-13th weeks of pregnancy)is indicative of possible DiGeorge syndrome, the pregnant woman should be referred to additional tests, particularly amniocentesis (obtaining amniotic fluid) in order to analyze fetal DNA for chromosomal abnormalities (deletions of the 22nd chromosome)[7].

Conflict of interests

There is no conflict of interests.

REFERENCES

1. Kondratenko I.V., BologovA.A. Primary immunodeficiencies – Moscow.: ID MEDPRAKTIKA-Moscow,2008, pp.23. (in Russian)

2. Allergology and Immunology. National leadership - Geotar-Media, 2009. (in Russian)

3. Bassett A.S., Chow E.W.C., Husted J. et al. Clinical features of 78 adults with 22q11 deletion syndrome// Am.J.Med.Genet. — 2015 – N 138A – P. 307 – 313.

4. Simptomy I sindromy v ehndokrinologii/Pod red. YU. I. Karachenceva. — 1-e izd. — H.: OOO «S.A.M.», Har'kov, 2006. — S. 67-68. — 227 s. — (Spravochnoe posobie). — ISBN 978-966-8591-14-3.

5. Bochkov, N.P. Nasledstvennye bolezni / N.P. Bochkov, E.K. Ginter, V.P. Puzyrev. – M. : GEHOTAR Media, 2012. – 565 s.

6. DiGeorge, A.M. Congenital absence of the thymus and its immunologic consequences: concurrence with congenital hypoparathyroidism / A. M. DiGeorge // BirthDefects Original Article Series. – 2008. – Vol. 4 (1). – P. 116–21.

7. DiGeorge, A. M. Discussion on a new concept of the cellular nasis of immunology/A. M. DiGeorge // J. Pediatr. – 2015. – Vol. 67 (5) (Suppl.). – P. 907–909.

РЕЗЮМЕ

Сенаторова А.С., Гончарь М.А., Логвинова О.Л.,
Стрелкова М.И.

КЛИНИЧЕСКИЙ СЛУЧАЙ СИНДРОМА ДИ ДЖОРДЖИ

Харьковский национальный медицинский университет

В статье освещен клинический случай синдрома Ди-Джорджи. Подробно изложены особенности течения заболевания, диагностический поиск, тактика лечения на госпитальном этапе и рекомендации по дальнейшему лечению в домашних условиях.

Ключевые слова: синдром Ди-Джорджи, первичный иммунодефицит, дети, лечение.

РЕЗЮМЕ

Сенаторова Г.С., Гончарь М.О., Логвинова О.Л.,
Стрєлкова М.І.

КЛІНІЧНИЙ ВИПАДОК СИНДРОМУ ДІ ДЖОРДЖІ

Харківський національний медичний університет

В статті висвітлено клінічний випадок синдрому Ді-Джорджі. Детально викладені особливості перебігу захворювання, діагностичний пошук, тактика лікування на госпітальному етапі та рекомендації щодо подальшого лікування вдома.

Ключові слова: синдром Ді-Джорджі, первинний імунодефіцит, діти, лікування.

Received: 03-Feb. – 2016
Accepted: 27-Mar. - 2016

PEDIATRICS

M.A Gonchar, E.V. Omelchenko, A.S. Senatorova, M.I. Strelkova, A.E. Silicheva, M.N. Ermolaev

THE STATE OF THE CARDIOVASCULAR SYSTEM IN CHILDREN WITH GASTROINTESTINAL DISORDERS

Kharkiv National Medical University, Ukraine

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].

• *Corresponding Author:*
***Olena Omelchenko**, MD, PhD, Associate rofessor, Department of Pediatrics 1 and Neonatology, Kharkiv National Medical University, Ukraine. E-mail: helenomelchenko@mail.ru*

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.

REFERENCES

1. Conroy, R. M., Pyörälä K., Fitzgerald, A.P. et al. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project // Eur. Heart J. – 2009. - № 24 (11). – 987-1003.

2. Kathiresan S. Genetics of human cardiovascular disease // Cell. – 2012. – Mar 16. – № 148(6). – P. 1242–57.

3. Mancia, G. Total cardiovascular risk: a new treatment concept //J. Hypertens. Suppl. – 2015. – № 24 (2). – P. 17–24.

4. Willerson, J. T., Ridker P.M. Inflammation as a cardiovascular riskfactor // Circulation. – 2014. – № 109 (21, Suppl. 1). – 112–110.

5. Verdecchia, P., Angeli F., Pittavini L. et al. Regression of leftventricular hypertrophy and cardiovascular risk changes in hypertensive patients // Ital. Heart J. – 2012. – № 5 (7). – 505–510.

6. Association between decreased vitamin levels and MTHFR, MTR and MTRR gene polymorphisms as determinants for elevated total homocysteine concentrations in pregnant women / P. R. Barbosa, S. P. Stabler, A. L. Machado [et al.] // Eur. J. Clin. Nutr. – 2011. – Vol. 62, № 8. – 1010–1021.

7. Genetic polymorphisms involved in folate metabolism and concentrations of methylmalonic acid and folate on plasma homocysteine and risk of coronary artery disease / M. Biselli, A. R. Guerzoni, M. F. de Godoy [et al.] // J. Thromb. Thrombolysis. – 2010. – Vol. 29, № 1. – 32–40.

РЕЗЮМЕ

Гончарь М.О., Омельченко О.В., Сенаторова Г.С., Стрелкова М.І., СілічеваА.Е., Єрмолаєв М.М.

СТАН СЕРЦЕВО-СУДИННОЇ СИСТЕМИ У ДІТЕЙ З ГАСТРОЕНТЕРОЛОГІЧНОЮ ПАТОЛОГІЄЮ

Харківський національний медичний університет

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.

ISSN 0123-4567

РЕЗЮМЕ

Гончарь М.О., Омельченко О.В., Сенаторова Г.С.,
Стрелкова М.І., СілічеваА.Е., Єрмолаєв М.М.

СОСТОЯНИЕСЕРДЕЧНО-СОСУДИСТОЙ СИСТЕМЫ У ДЕТЕЙ С ГАСТРОЭНТЕРОЛОГИЧЕСКОЙ ПАТОЛОГИЕЙ

Харьковский национальный медицинский университет

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.

Received: 13-Feb. – 2016
Accepted: 27-Mar. - 2016

INTER COLLEGAS JOURNAL, VOL. 3, No. 1 (2016)
ISSN 0123-4567

PEDIATRICS

M.O.Gonchar, O.O.Riga, A.D.Boychenko, I.Yu.Kondratova, V.O.Komova, N.R.Buzhynskaya

CHARACTERISTICS OF THE RISK FACTOR FOR CONGENITAL DISORDERS IN NEWBORNS

Kharkiv National Medical University, Ukraine

Summary. In order to objectify risk factors for cardiovascular diseases in newborns the study implied the assessment of mothers' medical records, labor characteristics, gestational age of 50 newborn infants who died of congenital heart diseases and 50 healthy newborns. The authors determined that fatal outcomeininfants with congenital heart diseases is 5.4 times more likely to occur in physiological pregnancythan innewborns with non-cardiac perinatal abnormalities. However, the risk of giving birth to a baby with congenital heart disease and unfavorable course increases in comorbidities, typical for pregnancy (2.6 times), acute respiratory viral infections during pregnancy (6.1 times), bacterial and / or viral infections before and during pregnancy (53 times)

Keywords: newborns, the risk of congenital heart defects

INTRODUCTION

Congenital heart disease (CHD) is the most common congenital disorder in newborns [1-3]. Critical CHD, defined as requiring surgery or catheter-based intervention in the first year of life, occurs in approximately 25 percent of those with CHD [4]. Although many newborns with critical CHD are symptomatic and identified soon after birth, others are not diagnosed until after discharge from the maternity clinic [5-8]. The risk of morbidity and mortality in infants with critical cardiac disorders increases inuntimely diagnosis and therefore timely referral to a tertiary center with expertise in treating these patients is essential [9-11]. Risks associated with pregnancy in women with congenital heart disease affect both the mother and her fetus. The obstetrician and cardiologist are consequently responsible for the welfare of two patients.Reparative surgery has substantially increased the number of females with congenital heart diseases who reach childbearing age. Successful operation before gestation is pivotal in reducing maternal and fetal risks. The risks of pregnancy after surgery are determined chiefly by the presence, type and degree of cardiac and vascular residua and sequelae.

The 2008 American College of Cardiology/American Heart Association guidelines for the management of adults with congenital heart disease and the 2011 European Society of Cardiology guidelines for management of cardiovascular disease during pregnancy included pregnancy recommendations for various congenital disorders [12, 13]. Women with congenital heart diseases are advised to consult a specialist in congenital heart disease in adults before becoming pregnant. The management plan should include labor and postpartum period. In women with congenital heart diseases, the risks of pregnancy to mother and fetus are related to the severity of the heart disease. The risks and predictors for maternal or fetal complications in women with congenital heart disease during pregnancy are as follows: pulmonary hypertension (pulmonary vascular disease), maternal cyanosis, low maternal functional class, history of arrhythmia, maternal anticoagulants [14-16].

Corresponding Author:

***Olena Riga**, MD, PhD, Professor, Department of Pediatrics 1 and Neonatology, Kharkiv National Medical University, Ukraine. E-mail: yeletskayaelena@gmail.com*

2 PURPOSES, SUBJECTS AND METHODS:

2.1 Purpose

The purpose of the study - to objectify risk factors of cardiovascular abnormalities in newborns

2.2 Subjects

Children who were born in the Regional Perinatal Center, Municipal Health Protection Institution "Regional Clinical Hospital - Accident and Emergency Medicine Center" during the secon half of 2013 and the first half of 2014 requiring intensive care.

The main group (the first group) was selected excluding children with genetic syndromes and congenital heart diseases due to mother's diabetes, excluding congenital heart diseases at post-mortem examination (Fig.1).

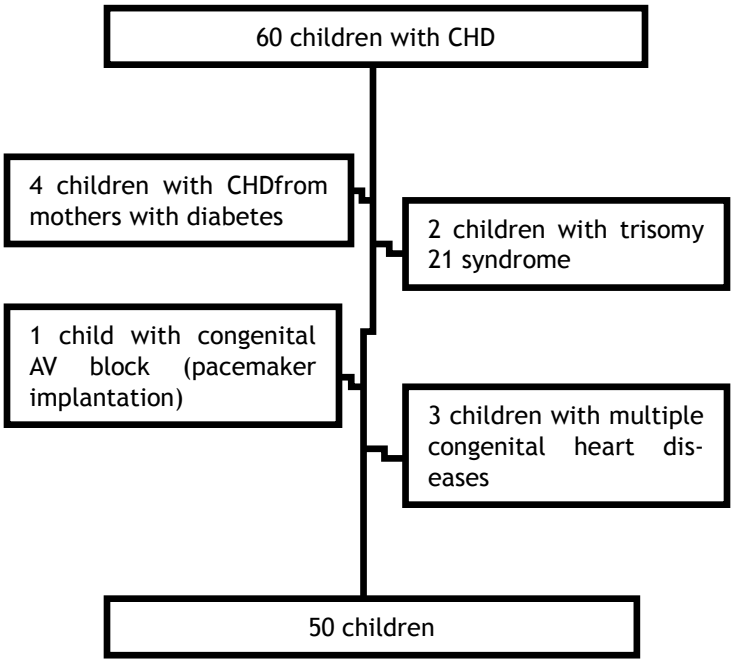

Fig.1. Schematic representation of congenital heart diseases in newborns

Control group (the second group) included 50 newborns of appropriate gestational age and body weight with perinatal abnormalities triggered by various factors.

2.3 Methods

Research design involved the study of mothers' medical records, labor characteristics, gestational age, body measeruments, comorbidities and other. Clinical and pathologic comparison was conducted for cases with fatal outcome.

3 RESULTS AND DISCUSSION

Distribution of children by sex, gestational age and body weight is given in Table 1. Thus, as can be seen from Table 1, the groups did not differ by sex, gestational age and body weight at birth and therefore are subject to evaluation.

Table 1

Main characteristics of groups under investigation, absolute (%)

Indicator	Group 1 n=50	Group 2 n=50	p
Male	29 (58)	33 (66)	0.4119
Gestational age **>37 weeks** **35-37 weeks** **<35 weeks**	 28 (56) 12 (24) 10 (20)	 23 (46) 15 (30) 12 (24)	 0.5675 0.6257 0.7500
Bodyweight **> 4000 g** **2500 - 4000 g** **<2500 g**	 2 (4) 38 (76) 10 (20)	 3 (6) 35 (70) 12 (24)	 0.7495 0.3427 0.7500
Days in the neonatal intensive care unit M±m	7±3.5	5±4.5	0.8046

CHD characteristics in Group 1 are presented in Table 2.

Table 2

Morphological characteristics of congenital heart diseases in newborns in groups under investigation.

Morphologicalcharacteristicsof CHD	Absolute	%
Isolatedventricularseptaldefect(VSD)	15	30.0
Isolatedatrialseptaldefect (ASD)	7	14.0
ASD and VSD	11	22.0
Atrial septal defect and open Botallo's duct	5	10.0
Hemodynamically relevant open Botallo's duct	4	8.0
Complex CHD (DORV, coarctation of the aorta, aorta stenosis and pulmonary artery; VSD; Pulmonary valve stenosis, VSD, ASD; Pulmonary valve stenosis, VSD)	4	8.0
Coarctationoftheaorta	2	4.0
Aortastenosis	1	2.0
Defects of aorta valve(bicuspid)	1	2.0
Total	50	100

Thus, septal defects rank a considerable proportion (66%) among other congenital heart diseases. The so-called "critical" heart diseases made up 16%.

Characteristics of pregnancy in mothers of the newborns under investigation are given in Table 3

Table 3

Main characteristics of groups under investigation (absolute, %)

Indicator	Group 1 n=50 abs.,%	Group 2 n=50 abs.,%	p
Pregnancy failure			
Anemia	14 (28.0)	20 (40.0)	0.2083
Moderate / severe preeclampsia	3 (6.0)	5 (10.0)	0.4628
Threatened abortion / miscarriage	17 (34.0)	12 (24,0)	0.2732
Premature rupture of membranes	5 (10.0)	8 (16.0)	0.3746
Placentalabruption	4 (8.0)	8 (16.0)	0.2217
Polyhydramnios/ oligohydramnios	3 (6.0)	3 (6.0)	1.0000
Combination of pregnancy failure	15 (30.0)	7 (14.0)	0.0500
Pregnancy without features	5 (10.0)	-	0.0500
Somatic and infectious diseases			
ARVI during pregnancy	38 (76.0)	17 (34.0)	0.0001
Chickenpox	1 (2.0)	-	0.6817
Chronic pyelonephritis	3 (6.0)	4 (8.0)	0.6960
Chronic gastritis	1 (2.0)	-	0.6817
Vulvovaginitis	2 (4.0)	2 (4.0)	1.000
Hepatitis C and B	2 (4.0)	1 (2.0)	0.5591
HIV	2 (4.0)	-	0.3390
Infections (viral and bacterial) total	49 (98)	24 (48.0)	0.0001
Congenitaldiseases	2 (4.0)	-	0.3390
Hypertension > II Degree	2 (4.0)	3 (6.0)	0.6474
Obesity I and II degree	2 (4.0)	3 (6.0)	0.6474
ICP andmentaldisorders	3 (6.0)	-	0.1768
Somatic noninfectious abnormalities (total)	9 (18.0)	6 (12.0)	0.4029

Significant differences in medical prenatal records of women who gave birth to children with CHD and with non-cardiac perinatal abnormalities wereobserved only in 4 indices: combination of pregnancy failure, pregnancy without features, ARVI during pregnancy, chronic bacterial and viral infections.

Presence of possible intergroup differences in the frequency of adverse perinatal factors was used for the assessment ofodds ratio for congenital heart disease risk in logistic regression models. The study implied the comparison ofGroup 1 children with congenital heart diseases and Group 2 children with non-cardiac perinatal abnormalities. Calculations of risk factors for congenital heart diseases are given in Table. 4.

Table 4

Odds ratio for perinatal adverse factors in newborns with congenital heart diseases

Sign	Basic data				Odds ratio (OR)	ln	SE	95% CI
	a	b	c	d				
Combination of pregnancy failure	15	35	7	43	2.6	0.96	0.51	0.94-7.31
Pregnancy without features	5	45	1	49	5.4	1.69	1.11	0.58-50.6
ARVI during pregnancy with fever	38	12	17	33	6.1	1.81	0.44	2.,53-14.9
Bacterial and viral infectious diseases	49	1	24	26	53.1	3.97	1.04	6.5-432.7

Note. a – Group 1 children with signs; b – Group 1 children without signs; c – Group 2 children with signs; d – Group 2 children without signs; OR- odds ratio;(ln) Napierian logarithm of odds ratio; SE - statistical error of ln; CI - confidence interval from 95% probability.

The obtained data coincide with the data published in the systematic review and the purpose of the analysis conducted for the first time was to prove that maternal fever of any naturein pregnancy triggers the development of congenital heart diseases. The study has not yet determined the impact of fever mechanisms in the development of certain types of congenital heart diseases. [17]

4 CONCLUSION

1. Assessment of medical records of mothers who gave birth to children with congenital heart diseases in comparison with withnon-cardiac perinatal abnormalities showed the following risk factors: combination of pregnancy failure (by 2,6 times); ARVI during pregnancy (by 6,1 times); infectious bacterial and/or viral diseases before and during pregnancy (by 53 times).

2. Congenital heart disease is 5.4 times more likely to occur in physiological pregnancy than in pregnancy with non-cardiac perinatal abnormalities.

REFERENCES

1. Tennant PW, Pearce MS, Bythell M, Rankin J. 20-year survival of children born with congenital anomalies: a population-based study. Lancet 2010; 375:649.

2. Bird TM, Hobbs CA, Cleves MA, et al. National rates of birth defects among hospitalized newborns. Birth Defects Res A ClinMolTeratol 2006; 76:762.

3. Canfield MA, Honein MA, Yuskiv N, et al. National estimates and race/ethnic-specific variation of selected birth defects in the United States, 1999-2001. BirthDefectsRes A ClinMolTeratol 2006; 76:747.

4. Oster ME, Lee KA, Honein MA, et al. Temporal trends in survival among infants with critical congenital heart defects. Pediatrics 2013; 131:e1502.

5. Wren C, Reinhardt Z, Khawaja K. Twenty-year trends in diagnosis of life-threatening neonatal cardiovascular malformations. ArchDisChildFetalNeonatalEd 2008; 93:F33.

6. Gregory J, Emslie A, Wyllie J, Wren C. Examination for cardiac malformations at six weeks of age. ArchDisChildFetalNeonatalEd 1999; 80:F46.

7. Samánek M, Slavík Z, Zborilová B, et al. Prevalence, treatment, and outcome of heart disease in live-born children: a prospective analysis of 91,823 live-born children. PediatrCardiol 1989; 10:205.

8. Peterson C, Ailes E, Riehle-Colarusso T, et al. Late detection of critical congenital heart disease among US infants: estimation of the potential impact of proposed universal screening using pulse oximetry. JAMA Pediatr 2014; 168:361.

9. Kuehl KS, Loffredo CA, Ferencz C. Failure to diagnose congenital heart disease in infancy. Pediatrics 1999; 103:743.

10. de-WahlGranelli A, Wennergren M, Sandberg K, et al. Impact of pulse oximetry screening on the detection of duct dependent congenital heart disease: a Swedish prospective screening study in 39,821 newborns. BMJ 2009; 338:a3037.

11. Eckersley L, Sadler L, Parry E, et al. Timing of diagnosis affects mortality in critical congenital heart disease. ArchDisChild 2015.

12. Warnes CA, Williams RG, Bashore TM, et al. ACC/AHA 2008 Guidelines for the Management of Adults with Congenital Heart Disease: Executive Summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing committee to develop guidelines for the management of adults with congenital heart disease). Circulation 2008; 118:2395.

13. European Society of Gynecology (ESG), Association for European Paediatric Cardiology (AEPC), German Society for Gender Medicine (DGesGM), et al. ESC Guidelines on the management of cardiovascular diseases during pregnancy: the Task Force on the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC). EurHeart J 2011; 32:3147.

14. Drenthen W, Boersma E, Balci A, et al. Predictors of pregnancy complications in women with congenital heart disease. EurHeart J 2010; 31:2124.

15. Siu SC, Sermer M, Harrison DA, et al. Risk and predictors for pregnancy-related complications in women with heart disease. Circulation 1997; 96:2789.

16. Siu S, Chitayat D, Webb G. Pregnancy in women with congenital heart defects: what are the risks? Heart 1999; 81:225.

17. Shi Q.Y. Congenital heart defects and maternal fever: systematic review and meta-analysis/Q Y Shi,J B Zhang,Y Q Mi,YSong,JMaandY L Zhang//Journal of Perinatology34, 677-682 (September 2014) |doi:10.1038/jp.2014.76

РЕЗЮМЕ

Гончарь М.О., Ріга О.О., Бойченко А.Д., Кондратова І.Ю., Комова В. О., Бужинська Н.Р.

ХАРАКТЕРИСТИКА ФАКТОРІВ РИЗИКУ ДЛЯ РОЗВИТКУ ВРОДЖЕНИХ ВАД СЕРЦЯ

Харківський національний медичний університет

З метою об'єктивізації факторів ризику виникнення серцево-судинної патології у новонароджених визначено анамнез матері, особливості пологів, гестаційний вік у 50 новонароджених дітей, які померли від вроджених вад серця та у 50 здорових новонароджених. Авторами визначено, що народження дітей з вродженими вадами серця, які мають критичний перебіг, у 5,4 разів частіше відбувається при нормальному перебігу вагітності ніж народження дітей з перинатальною патологією некардіального характеру. Але ризик народити дитину з вродженими вадами серця та несприятливим перебігом підвищується якщо у жінок є сполучення патологічних станів, характерних для вагітності (у 2,6 разів); ГРВІ під час вагітності (у 6,1 разів); наявність інфекційних бактеріальних та/або вірусних захворювань до та під час вагітності (у 53 рази).

Ключові слова: новонароджені, ризик вроджених вад серця

РЕЗЮМЕ

Гончарь М.А., Рига Е.А., Бойченко А.Д., Кондратова И.Ю., Комова В. А., Бужинская Н.Р.

ХАРАКТЕРИСТИКА ФАКТОРОВ РИСКА ДЛЯ РАЗВИТИЯ ВРОЖДЕННЫХ ПОРОКОВ СЕРДЦА

Харьковский национальный медицинский университет

С целью объективизации факторов риска возникновения сердечно-сосудистой патологии у новорожденных изучен анамнез матери, особенности родов, гестационный возраст у 50 новорожденных детей, умерших от врожденных пороков сердца и у 50 здоровых новорожденных. Авторами установлено, что рождение детей с врожденными пороками сердца, которые имеют критический исход, в 5,4 раза чаще происходит при нормальном течении беременности, чем рождение детей с перинатальной патологией некардиального характера. Но риск родить ребенка с врожденными пороками сердца и неблагоприятным течением повышается, если у женщин имеет место сочетание патологических состояний, характерных для беременности (в 2,6 раз), ОРВИ во время беременности (в 6,1 раз), наличие инфекционных бактериальных и /или вирусных заболеваний до и во время беременности (в 53 раза).

Ключевые слова: новорожденные, риск врожденных пороков сердца

DERMATOLOGY

A.M. Dashchuk, V.V. Pochernina

TOLL-LIKE RECEPTORS AND THEIR ROLE IN THE DEVELOPMENT OF PSORIASIS

Kharkiv National Medical University, Ukraine

Abstract: The study deals with determination of the role of TOLL-like receptors 4 and 9 inthe development of psoriasis. Patients with psoriasis were shown to have an increase in production and hypersecretion of pro-inflammatory biomarkers, namely TLR4 and TLR9-positive cellsby epithelial cells. Respective TLR4 and TLR9-positive cells were detectedboth in the areas of the skin affected by psoriatic rash and in the intact skin. However, the number of the respective cells in the affected skin areas is greater than in the intact skin.

Key Words: psoriasis, TOLL-like receptors, chronic dermatoses.

INTRODUCTION

Psoriasis is a common, chronic skin disease, affecting approximately 2% of the population. Most scientists refer to the common clinical variant termed psoriasis vulgaris, which affects approximately 85 to 90% of all patients with the disease. Psoriasis is associated with a high degree of morbidity; patients are embarrassed about the appearance of their skin, and there are side effects of medications. Moreover, patients with psoriasis, like those with other major medical disorders, have reduced levels of employment and income as well as a decreased quality of life.
The combined costs of long-term therapy and social costs of the disease have a major impact on health care systems and on the society in general.
According to the International Federation of Psoriasis Association the prevalence of psoriasis in the world is not the same, it depends on the region and ranges from 1.2% to 5%, and the average incidence is approximately 3% of the general population [13-15].

• ***Corresponding Author:***
***Andrey Dashchuk**, MD, PhD, Professor, Head of the Department of Dermatology, Venereology and AIDS, Kharkiv National Medical University, Ukraine. E-mail: kafedraderma@i.ua*

The interest in the study has been stimulated by theidentification of increased amount of Toll-receptor in the skin of patients with psoriasis.
TOLL-like receptors (TLRs) are a class of conserved receptors that recognize pathogen-associated microbial patterns. These receptors are also expressed in the skin cells including keratinocytes, melanocytes and Langerhans cells. The system of innate recognition formed during vertebrate evolution, implemented using effector cells involved in the first line of defense against all antigenically foreign compounds. These include the following types: epithelial cells, macrophages, dendritic cells, granulocytes, mast cells, NK cells, and others. These effectors have phagocytic and killer activity, provide network signals, activating and directing antigen-specific response by cells of the adaptive immune system. These cells serve as a bridge between pathogen-associated molecular structures (PAMPs) and antigen-specific cells of the adaptive immune response, broadcast signals of specific genetically encoded receptors (PRRs) in the soluble mediators that bind to the T and B cells via specific cytokine / chemokine receptors. One of the key events is the synthesis of complex pro-inflammatory cytokines stimulating most stages of inflam-

mation and providing the activation of various cell types involved in the maintenance and regulation of inflammation. Because of several functionally different classes of PRRs most well-characterized Toll-like receptors (TLRs) relate to the signaling PRRs and are an important component of the innate immune system. Numerous experimental studies, as well as accumulated findings of clinical practice of compelling evidence suggest the key role of Toll-like receptors in the development of immune diseases [1,2,3].

Table 1

Classification TLRs of human depending on the chromosomal localization of the genomic structure and amino acid sequences.

SubfamilyTLRs	*The members of the subfamilies*
TLR2	TLR1, TLR2, TKR6, TLR10
TLR3	TLR3
TLR4	TLR4
TLR5	TLR5
TLR9	TLR7, TLR8, TLR9

The role and function of TLRs in human skin has become a subject of study relatively recently. In the foreign literature there are few data on the presence of different TLRs in the different layers of the epidermis keratinocytes in healthy individuals [4-6]. According to B. Baker et al., TLRsexpressed on cells of the epidermis are subject to change as we move from the basal keratinocytes to horny layer of the epidermis [7]. According to E. James et al., keratinocytes of the skin of healthy individuals express TLR1, TLR2, TLR4 and TLR5. A. Pivarcsi established the presence of TLR2 and TLR4 in all layers of the epidermis of healthy individuals [6]. Mempel M. et al. showed that the culture of primary keratinocytes in healthy person produces TLR1, TLR2, TLR3, TLR5 and TLR9. Simultaneously, TLR4, TLR6, TLR7 and TLR8 were found in the same culture [8]. Some authors [5] believe that TLRs activated keratinocytes are able to initiate the adaptive immune response. In particular, S. Akira found that supernatant TLR-stimulated keratinocytes triggered dendritic cell maturation [9]

The role of TLRs in psoriasis is not well understood. E. Begone et al.[10] identified marked TLR1 expression on keratinocytes of the basal layer of the epidermis in patientswith psoriasis. B. Baker determined marked expression of TLR2 in the upper ranks of the spinous layer of the epidermisin the affected skin of patients with psoriasis, while in the skin of healthy subjects, and the unaffected skin of patients with psoriasis TLR2 expression was detected in the lower ranks of the thorny layer, located above the basal layer. J. Curry et al. found a decrease in TLR5expression in keratinocytes of the basal layer of the epidermis of the skin affected with psoriasis compared with the skin of healthy individuals [11]. Katunina et al. described patients with psoriasis who were shown to have dermis expression of TLR2 and TLR4 in the endothelium of blood vessels, cells and histiocytic macrophage number of inflammatory infiltrates, epithelial cells in the sweat glands and the outer root sheath of hair follicles [12].

2 PURPOSES, SUBJECTS AND METHODS:

2.1 Purpose

The purpose of the present study was to examine the role of toll-like receptor in psoriasis

2.2 Subjects

The study involved 25 patients with ordinary psoriasis. Patients underwent biopsy study of the skin affected by psoriatic rash, as well as areas with intact skin. Comparison of immunohistochemical findings was followed by the assessment of biopsy samples taken from 5 healthy individuals.

2.3 Methods

Biopsy samples were evaluated by standard histological processing: fixed in 10% formalin solution exposed to histological wiring by dehydration in ethanol and pouring paraffin.

The study of the number and distribution of TOLL-like receptor of Class 4 (CD284) and 9 (SD289) (TLR4, TLR9) in the structures of the skin was performed by immunohistochemistry using monoclonal antibodies to TLR4 and TLR9

produced by “Abbiotec” (USA), streptavidin-biotinylated secondary antibodies Novocastra Peroxidase Detection System Production “Leica Microsystems” (United Kingdom). Paraffin sections were spread on slides coated with polylysine. The reaction was assessed according to the protocols attached to the employed monoclonal antibodies. High temperature antigen unmasking was performed by boiling sections in citrate buffer (pH 6.0) in a microwave oven at the maximum power of 900 W for three cycles of 5 minuteswith one-minute break. Cooled preparations were washed in Tris buffer solution (pH 7.54-7.58), treated with 0.3% peroxide solution conduit to methanol (1: 1) to prevent endogenous peroxidase activity. Incubations with primary antibodies were performed for 60 min at 23°C and30 min for secondary antibodies.

Background staining was performed in an incubator at 37°C with Mayer's hematoxylin contrasting sections. Immunohistochemicalagentswere obtained with a coverslip and examined using a light microscope Leica DM4000V (Germany). Calculation of the area of expression of toll-like receptors in the epidermis and dermis was carried out using a computer image analysis program ImageJ. In the epidermis cell area was determined with a positive response, which is expressed in square pixels. The content of the dermis toll-like receptor was determined by calculating the area of vascular endothelium where receptor expression was observed.

Conflict of interests

There is no conflict of interests.

3 RESULTS AND DISCUSSION

The surface layers of the epidermis, as in patients with psoriasis and healthy subjects from the control group, had only some cells with weakly positive staining. Also there were areas in the skin with no signs of edema and adverse reactions to TLR4 and TLR9.

Single TLR4 and TLR9-positive cells were observed in the dermis in small clusters of inflammatory cells. In positive substrate reaction there were fine granules with light to moderate staining in the nucleus and in the cytoplasm of positive cells.

In psoriatic plaques epidermis layeris significantly thickened with an increased number of TLR4 and TLR9-positive cells. The study identified the following pattern: TLR4 and TLR9-positive cells in the epidermis wereobserved in the areas of edema with a considerably smaller amount in the sites of compact settlement of epithelial cells.

The intact skin of patients with psoriasis was found to have more active focal expression of TLR4 and TLR9in the epidermis. The topography of such sites contained increased papillae or formed papillae. In the epidermis they were determined by positive staining of epithelial cells of the entire epidermis.

Active expression of the marker was observed in other areas involving the epidermis. Moderate positive staining was used as in the few cells of prevascular inflammatory infiltrates papillary dermis.

TLR4 and TLR9 expression in the epidermis of healthy individuals in the control group was most significant in the basal and prickle layerof the skin.

Patients with psoriasis were found to have an increase in production and hypersecretion of pro-inflammatory biomarkers, such as TLR4 and TLR9-positive cellsby epithelial cells of the skin. Respective TLR4 and TLR9-positive cells were identifiedboth in the areas of the skin affected by psoriatic rash and in the intact skin. However, the number of the respective cells in the affected skin areas was greater than in the intact skin.

4 CONCLUSIONS

Expression of TLR-4 and TLR9-positive cells suggests that an important link in the pathogenesis of the dermatosis is antigenic stimulation of immune cells that leads to the development of the inflammatory process in the superficial layers of the skin.

REFERENCES

1. Clark R., Kupper T. (2005) Old meets new: the interaction between innate and adaptive immunity, J Invest Dermatol, 125, 629—37.

2. Haitov R.M., Ignat'eva G.A., Sidorovich I.G. (2010) Immunology. Norm and Pathology: Textbook, M.: OAO «Izdatel'stvo «Medicina».

3. Lebedev K.A., Ponyakina I.D. (2009) Immunology of receptors (Integrated Immunology), M.: Knizhnyjdom «LIBROKOM», 256.

4. Valins W., Amini S., Berman B. (2010) The Expression of Toll-like Receptors in Dermatological Diseases and the Therapeutic Effect of Current and Newer Topical Toll-like Receptor Modulators, J ClinAesthetDermatol, 20—29.

5. James E., Mclnturff R., Modlin J. K.(2005) The role of toll-like receptors in the pathogenesis and treatment of dermatological disease, J Invest Dermatol, 8.

6. Pivarcsi A., Bodai L., Rethi B. et al. (2003) Expression and function of Tolllike receptors 2 and 4 in human keratinocytes, IntImmunol, 721—730.

7. Baker B.S., Ovigne J.M., Powles A.V. et al. (2003) Normal keratinocytes express Toll-like receptors (TLRs) 1, 2 and 5: Modulation of TLR expression in chronic plaque psoriasis. Br J Dermatol, 148, 670—679.

8. Mempel M.,Voelcker V., Kollisch G. et al (2003) Toll-like receptor expression in human keratinocytes: Nuclear factor kappaB controlled gene activation by Staphylococcus aureus is toll-like receptor 2 but not toll-like receptor 4 or platelet activating factor receptor dependent, J Invest Dermatol,1389—1396.

9. Akira S., Takeda K., Kaisho T. (2001) Toll-like receptors: critical proteins linking innate and acquired immunity, Nature Immunol, 2, 675—680.

10. Btgone E., Michel L., Flageul B. et al. (2007) Expression, subcellular localization and cytokinic modulation of Toll-like receptors (TLRs) in normal human keratinocytes: TLR2 up-regulation in psoriatic skin,Europ J Derm, 497—506.

11. Curry J.L., Qin J.Z., Bonish B., et al (2003), Innate immune-related receptors in normal and psoriatic skin, Arch Path Lab Med, 178—186.

12. Katunina O.R. et al.(2011) Functions of Toll-like receptors as an inborn immunity component and their participation in the pathogenesis of dermatoses of different etiologies, J Exp Me, 18-25.

13. Fedorenko O.E. Clinical exper ence of psoriasis therapy, Ukrainian Journal of Dermatology, Venerology, Cosmetology, 1(44, 59-62.

14. Harchenko T.(2012) Psoriasis in Ukraine: modern approaches for solutions problems, Ukrainian Medical Journal. – 01.10.2012. [Ehlektronnaya publikaciya] www.umj.com.ua – C 1-3.

15. Wolkenstein P. (2009) Psoriasis in France and associated risk factors: results of a case control study based on a large community survey, P. Wolkenstein, J. Revuz, J.C. Roujeau, et al, Dermatology, Vol.218., 103-109.

РЕЗЮМЕ

Дащук А.М., Почерніна В.В.

ТОLL-ПОДІБНІ РЕЦЕПТОРИ І ЇХ РОЛЬ У ПАТОГЕНЕЗІ ПСОРІАЗУ

Харківськийнаціональниймедичнийуніверситет

Обговорюється вивчення TOLL-подібнихрецепторів 4 і 9 типу в шкірі хворих на псоріаз (в інтактній та в ураженій шкірі). У хворих на псоріаз встановлена гіперпродукція і гіперсекреція епітеліоцитами шкіри прозапальних біологічних маркерів, зокрема TLR4 і TLR9- позитивних клітин. Відповідні TLR4 і TLR9-позитивні клітини визначаються як в уражених псоріатичними висипаннями ділянках шкіри, так і в інтактнній шкірі. Але кількість відповідних клітин в ділянках ураженої шкіри більше, ніж інтатктной.

Ключові слова: псоріаз, TOLL-подібні рецептори, хронічні дерматози.

РЕЗЮМЕ

Дащук А.М., Почернина В.В.

ТОLL-ПОДОБНЫЕ РЕЦЕПТОРЫ И ИХ РОЛЬ В ПАТОГЕНЕЗЕ ПСОРИАЗА

Харьковский национальный медицинский университет

Обсуждается изучение TOLL-подобных рецепторов 4 и 9 типа в коже больных псориазом (в интактной коже и в пораженной коже). У больных псориазом установлена

гиперпродукция и гиперсекреция эпителиоцитами кожи провоспалительных биологических маркеров, в частности TLR4 и TLR9-положительных клеток. Соответствующие TLR4 и TLR9-положительные клетки определяются как в пораженных псориатическими высыпаниями участках кожи, так и в интактной коже. Но количество соответствующих клеток в участках пораженной кожи больше, чем в интатктной.

Ключевые слова: псориаз, TOLL-подобные рецепторы, хронические дерматозы

Received: 07-Jan. – 2016
Accepted: 25-Feb. - 2016

INTER COLLEGAS JOURNAL, VOL. 3, No. 1 (2016)
ISSN 2409-9988

DERMATOLOGY

Bilovol A.M., Tkachenko S.G., Volovik O.V.

APPLICATION OF DERMATOSCOPY IN THE MANAGEMENT OF SCABIES

(Case)

Kharkiv National Medical University, Ukraine

Abstract: *The article presents a case report on the employment of entomodermoscopy in diagnosis of scabies. Clinical studies of scabies using dermatoscopy provide evidence that the new method helps to improve therapy and reduce the term of medication. As of today dermoscopic patterns of scabies have been identified. We presented our experience of dermatoscopy employment in the management of microscopically negative scabies and presented a clinical case of dermoscopically diagnosed scabies. As a result of treatment, the patient has been shown to have a dramatic improvement. Presented clinical case has shown effectiveness and importance of entomodermoscopy in the improvement of parasitosis diagnosis and patient's compliance.*

KeyWords: *scabies, dermoscopy, entomodermoscopy.*

INTRODUCTION

Dermatoscopy ranks high among new diagnostic techniques nowadays. This method helps to diagnose scabies quickly and does not require special preparation of the patient. Advantages of this method also comprise non-invasive nature of the procedure, patient comfort and portability of the equipment. Clinical studies of scabies using dermatoscopy provide evidence that the new method can optimize therapy and adjust the terms of medication. This is important to minimize the risks of excessive or insufficient treatment, reduce the risk of side effects and promote patient's compliance, particularly in cases of residual itching after therapy [1, 2].

Previous studies described the following dermoscopic patterns of scabies: delta and ovoid structures, similar to "jet trails" providing a possibility to diagnose parasitosis and due to non-invasive nature it is well-perceived by the patient. Dermatoscopy can identify mite eggs, excrement and burrows in the skin [3, 4].

• ***Corresponding Author:***
Svitlana Tkachenko, *MD, PhD, Professor, Department of Dermatology, Venereology and Cosmetology, Kharkiv National Medical University, Ukraine. E-mail: svetmail@mail.ru*

The first reports on dermatoscopy in diagnosis of scabies were published by Argenziano et al. [5]. Their study showed the abovementioned dermoscopic pattern resembling "jet trails" in 93% of patients infected by Sarcoptes scabiei var. hominis. Microscopic studies showed that the brown triangle corresponds to the anterior part of the mite (mouth and anterior pair of legs). Posterior part of the mite is invisible that is why the abdomen and posterior pair of legs appears translucent. The mite burrow corresponds to "jet trails" and may contain feces seen as small brown dots. According to their recommendations, in crusted scabies (scabies crustosa) at 10-fold magnification multiple mites can be identified as brown-gray triangles at the end of a whitish winding burrow leaving no doubt as to the diagnosis. More recent studies confirmed these findings and fixed the value of dermatoscopy in diagnosis of scabies [6, 7].

CASE DESCRIPTION:

A 36-year-old single male was admitted to the in-patient department of Kharkiv City Clinical Hospital of Skin and Venereal Diseases No.5 with diagnosis of allergic dermatitis. On admission he presented with intense itching for a month, which became worse in the evening. He was not

able to provide any apparent reason for itching. Three months ago he consulted an outpatient dermatologist and was referred to microscopic studies to identify scabies which gave negative results.

The diagnosis allergic dermatitis was made.

The following treatment was administered: loratadine 1 table once a day No. 14; 10% calcium gluconate solution 10 ml IV once a day No.10; Clemastine solution 2 ml IM two times a day No.10, topical applications of methylpr - dnisolone aceponate cream two times a day. The patient reported a decrease in itching during treatment, but the character and intensity of symptoms resumed after the course of therapy.

Status localis: skin is light beige, turgor and elasticity are within norm, skin type II. There are some diffuse bright pink rounded and elongated spots up to 5 mm in diameter and bright pink papules of 3-5 mm in diameter on the skin of trunk and extremities. He is also found to have linearly arranged papules and vesicles on the skin of the corpus penis. Some of the lesions are covered with hemorrhagic crusts.

The results of microscopical examination for Sarcoptes scabiei are negative.

Dermatoscopy findings. Dermatoscopy examination was carried out by "Aramo" video dermatoscope at 10-fold, 20-fold and 60-fold magnification. Dermatoscopy of the abdomen showed some paired follicular papules, covered with hemorrhagic crusts (Figure 1).

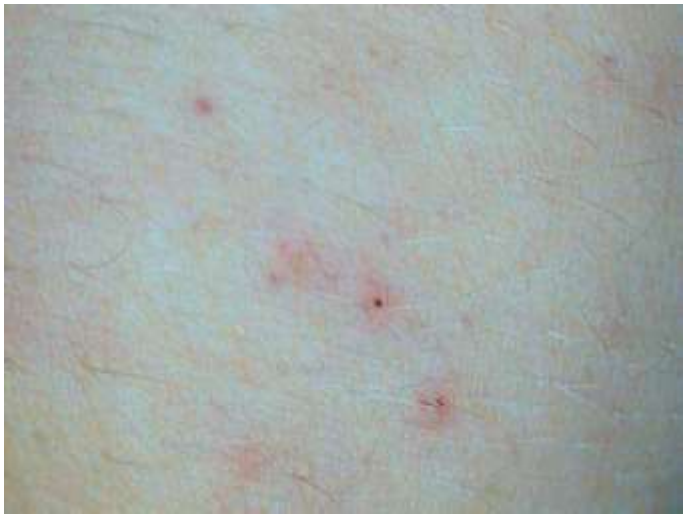

Fig.1.Paired follicular papules on the belly skin×10

The mite burrow with several holes linearly located on papulovesicular lesions (Figure 2) was detected by dermatoscopy of the penis. Dermatoscopy of the buttocks determined typical mite burrow filled with liquid.

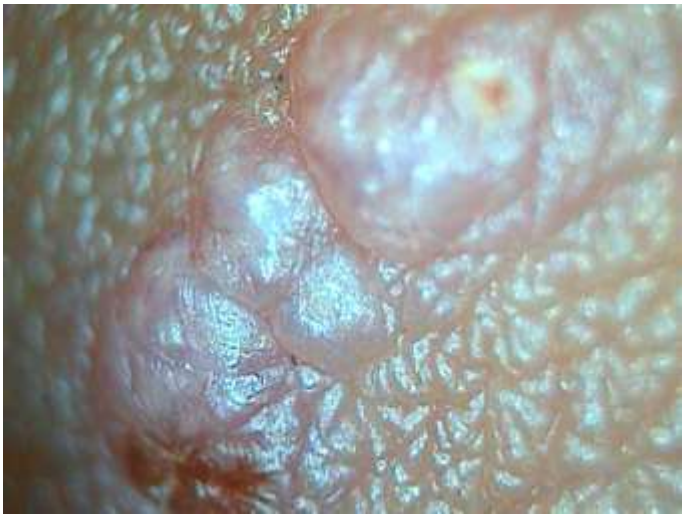

Fig.2.Themite burrowthe skin of penis×60

The body of mite was visualized at the end of the burrow. Examination also revealed “jet trails” pattern in the form of small brown dots which usually contain feces of Sarcoptes scabiei (Figure 3).

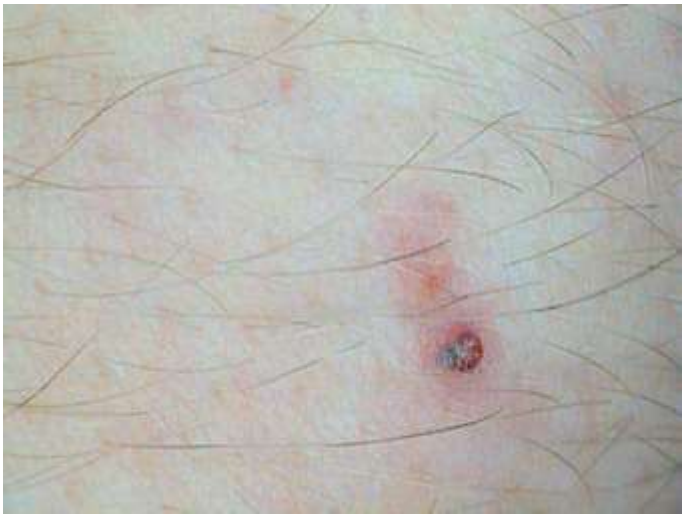

Fig. 3. The borrow on the skin of buttocks ×20.

According to dermatoscopy findings, the patient was prescribed ex juvantibus treatment of scabies: fixed combination of piperonyl butoxide and esdepallethrine as aerosol topically, disinfestation of linen and clothes.

As a result of treatment, the patient reported a significant reduction in itching as early as in the first night and complete disappearance of subjective symptoms for three days. Eruptions on the skin completely resolved within five days.

CONCLUSIONS

Nowadays dermatoscopy is rarely used by dermatologists to manage scabies. However, identified dermatoscopic patterns give a possibility to diagnose this parasitosis. The presented case report demonstrates practical effectiveness of entomodermoscopy for in-patient management of scabies. The study confirms greater sensitivity of dermatoscopy in diagnosis of scabies as compared to visual inspection and microscopic examination. In our opinion, dramatic improvement during treatment is due to elimination of sensitizing by previous antiallergic treatment. Therefore, immobilization and destruction of the parasite were accompanied by a very rapid disappearance of subjective and objective manifestations of dermatosis. Our study has shown the effectiveness and significance of dermatoscopy in diagnosis of scabies in practical clinical work.

REFERENCES

1. Francesco Lacarrubbaet all.(2010) Use of dermatoscopy and videodermatoscopy in therapeutic follow-up: a review, International Journal of Dermatology , 49, 866–873.
2. Zalaudek I, Giacomel J, Cabo H, et al. (2008) Entodermoscopy: a new tool for diagnosing skin infections and infestations, Dermatology, 216, 14–23.
3. Dermatoscopy in clinical practice. Pod red. N.N.Potekayev., M.: Studiya MDV, 144.
4. Gentiane Monsel, Olivie rChosidow (2012). Management of Scabies, Skin Therapy Letter, 2012 17(3).
5. Argenziano G, Fabbrocini G, Delfino M. (2007) Epiluminescence microscopy. A new approach to in vivo detection of Sarcoptes scabiei, Arch Dermatol., 133, 751–753.
6. Bauer J. et all. (2001) Nodular scabies detected by computed dermatoscopy, Dermatology, 203, 190–191.
7. Prins C et all. (2004) Dermoscopy for the in vivo detection of sarcoptesscabiei, Dermatology, 208, 241–243.

РЕЗЮМЕ

Біловол А.М., Ткаченко С.Г., Воловік О.В.

ВИКОРИСТАННЯ ДЕРМОСКОПІЇ У ВЕДЕННІ КОРОСТИ

Харківський національний медичний університет, Україна

Стаття є описом клінічного випадку практичного використання ентомодермоскопії в діагностиці корости. Результати клінічних досліджень корости з використанням дермоскопії показали, що новий метод сприяє оптимізації терапії та скорочує строки використання ліків. На сьогодні вивчені дермоскопічні паттерни корости. Ми навели свій власний досвід використання дермоскопії у менеджменті мікроскопічно негативної корости та представили клінічний випадок дермоскопічно діагностовано корости. В результаті скабіцидного лікування пацієнт продемонстрував драматичне покращення. Наведений клінічний випадок показав корисність і значимість ентомодермоскопії у покращені діагностики паразитоза та комплайнса пацієнта.

Ключові слова: короста, дермоскопія, ентомодермоскопія

РЕЗЮМЕ

Беловол А.Н, Ткаченко С.Г., Воловик О.В.

ИСПОЛЬЗОВАНИЕ ДЕРМОСКОПИИ В ВЕДЕНИИ ЧЕСОТКИ

Харьковский национальный медицинский университет, Украина

Статья представляет собой описание клинического случая практического использования энтомодермоскопии в диагностике чесотки. Результаты клинических исследований чесотки с использованием дермоскопии показали, что новый метод способствует оптимизации

терапии и сокращать сроки применения лекарств. На сегодняшний день описаны дермоскопические паттерны чесотки. Мы представили свой опыт использования дермоскопии в менеджменте микроскопически негативной чесотки и представили клинический случай дермоскопически диагностированной чесотки. В результате скабицидного лечения пациент продемонстрировал драматическое улучшение. Представленый клинический случай показал полезность и значимость энтомодермоскопии в улучшении диагностики паразитоза и коплайнса пациента.

Ключевые слова: чесотка, дермоскопия, энтомодермоскопия

Received: 21-Feb. – 2016
Accepted: 29-Mar. - 2016

GYNECOLOGY

I.M.Shcherbina, I.U.Plakhotnaya, N.V.Kapustnik, O.O.Dynnik

DIAGNOSTIC ROLE OF CHANGES IN LOCAL AND SYSTEMIC IMMUNITY INDICES IN PREGNANT WOMEN WITH BACTERIAL INFECTIONS

Kharkiv National Medical University, Ukraine

Abstract: The article presents predictors of neonatal complications basing on comprehensive clinical and immunological examination of pregnant women. The study included 35 pregnant women, divided into two groups. The first (main) group comprised 25 patients with intrauirtrine infections (IUI) in newborns in the early neonatal period and the second (control) group amounted for 10 patients without IUI in newborns. Quantitative study of proinflammatory cytokine levels in the serum of pregnant and posterior vaginal vault content showed a significant increase in IL-8 (16.73 pg /ml,p =0.021) and IL-6 (38.4 pg /mL, p =0.032) in the blood serum of pregnant women p=0.032), who gave birth to children with IUI. Cytokine levels in the contents of posterior vaginal vault was also increased in the first group of pregnant: IL-6 (89.41mg /g) andIL-1β (157.2g / g) (p <0.05). Therefore the results of studies to determine immunological markers of inflammation give a possibility to predict early neonatal complications in pregnant women who are at risk for IUI, thus reducing the risk of infection in newborns by timely preventive and therapeutic measures.

Key Words: cytokines, intrauterine infection, C-reactive protein, immunological markers.

INTRODUCTION

Reproductive loss and miscarriage in intrauterine infection are one of the pressing challenges in perinatology. Risk factors for abnormal conditions in fetus include infectious and inflammatory diseases of women during pregnancy. Intrauterine infection (IUI) is often caused by specific flora in the birth canal of the mother [1].

The role of the immune system in vaginal infection currently remains disputable. As the number of studies suggest, changes invaginal infections occur in various parts of the immune system [3].Chronic persistent infection in the mother's body helps to maintain a consistently high level of innate immune protection factors in an active state due to exposure to Toll-receptor system cells. Receptors activation triggers cytokine cascade which starts inflammatory response [5].

• *Corresponding Author:*
***OleksandraDynnik**, MD, PhD, Department of Obstetrics and Gynecology № 1, Kharkiv National Medical University, Ukraine. E-mail: aleksa_dynnik@rambler.ru*

Despite recent advances inprevention and treatment, IUI incidence in infants continues to grow. Early diagnosis is not always possible. Symptomsof infectionare oftennon-specific and laboratory diagnosis is time-consuming.

Thus, timely prediction, diagnosis and treatment can significantly reduce the risk of serious complications in infants with IUI.

2 PURPOSES, SUBJECTS AND METHODS:

2.1 Purpose

Prediction of neonatal complications based on a comprehensive clinical and immunological examination of pregnant women.

2.2 Subjects

The study included 35 pregnant women, divided into two groups.The first (main) group comprised 25 patients with IUI in newborns in the early neonatal period; the second (control) group amounted for 10 patients without IUI in newborns.

2.3 Methods

All the patients underwent conventional range of examina-

tions. The state of innate immunity was assessed by the content of cytokines in serum and discharge from the posterior vaginal vault.Venous blood was analyzed for acute phase proteins (C-reactive protein (CRP), procalcitonin). The study implied the employment of enzyme immunoassay. Optical density was analyzed with "Microplate reader Model 550" photometer.

Conflict of interests

There is no conflict of interests.

2 RESULTS AND DISCUSSION

Proinflammatory cytokines, particularly IL- 1ß, (TNF) α, IL-6, IL-8, IL-10, were also evaluated.

The age of pregnant women under investigation ranged from 22 to 39 years and averaged 31 ± 0.5 and 28 ± 0.5, respectively. Examination for extragenital diseases showed a statistically significant increase in the incidence of chronic ENT diseases (32.3%), chronic kidney diseases (25.1%), cystitis (30.2%) ($p < 0.05$).

The main grouppatients were more often found to have opportunisticvulvovaginalinfection (43.5%), herpes simplex virus carrier status (42.1%), candidiasis (35%), ureaplasma (36.4%) ($p < 0.05$). Evaluation of IUI rate in the first group showed such severe conditions as congenital pneumonia (60.3%) and sepsis (14%).

Quantitative study of proinflammatory cytokine levels in the serum of pregnant and posterior vaginal vault content showed a significant increase in IL-8 (16.73 pg /ml, $p = 0.021$) and IL-6 (38.4 pg/mL, $p = 0.032$) in the blood serum of pregnant women $p=0.032$), who gave birth to children with IUI.

Cytokine levels in the contents of posterior vaginal vaul were also increased in the first group of pregnant: IL-6 (89.41mg/g) and IL-1ß (157.2g/g) ($p < 0.05$).

Evaluation of the content of acute phase proteins showed an increase in CRP to 19.7 mg/ml ($p = 0.07$), while in the second group its level was 2.6 mg/ml, which corresponds to the normal physiological range. Acute phase protein content was also found to be increased in the first group newborns, amounting to12.1mg/L. CRP indices in the second group corresponded to age norm, and did not exceed 5mg/l.

4 CONCLUSIONS

The immune system in pregnant should be adapted to semiallogenic fetus and be active against different pathogens of bacterial and viral infections [3]. Cytokines perform one of the important functions of the immune responses, as they are one of the earliest mediators of inflammation being produced in the foci of inflammation for a long time [2].

Our study shows an increase in pro-inflammatory cytokines IL-6, IL-8, and the local- IL-1ß, IL-6 at the systemlevel. Furthermore, 48% of pregnant women with premature abortion were found to have increased IL-6, IL-8, IL-1ß content [4].

Thus, our findings concerning determination of immunological markers of inflammation give a possibility to predict the development of early neonatal complications in pregnant women who are at risk for IUI, consequently reducing the risk of infection in newborns by means of timely-preventive and therapeutic measures.

REFERENCES

1. Sidorova I.S. (2012) Intrauterine infection: prenatal care, delivery and postpartum period, M.:MEDpressinform, 160.
2. Carrol E.D., Payton A., Payene D., Miyajima F.,Chaponda M., Mankhambo L.A.et all. (2014) The IL1RN promoters 4251961 correlates with IL-1 receptors antagonist concentrations in human infection and is differentially regulated by GATA-1 J.Immunol. 2014; 186(4):2329-35.
3. Cardenas I., Aldo P., Koga K., Means R., Lang S.H., Mor G. (2011)Subclinscal viral infection in pregnancy lead to inflammatory process at the placenta with non-lethal fetal damage. Am. J. Reprod.Immunol. 2011; 64: 425, adstr. S314.
4. Mc.Cormick J., Bocking A., Reid G. Importance of vaginal mycrobes in reproductive health. Reprod.

Sci. 2012; 19(3): 235-42.

5. Schaaf B.M., Boehmke F., Esnaashari H., Seitzer U., Kothe H., Maas M. Et al. Pneumococcal septic shock is associated with the interleukin -10-1082 gene promoter polymorphism. Am. J. Respir. Crit. CareMed. 2010; 178(4): 435-78.

РЕЗЮМЕ

Щербіна І.М., Плахотна І.Ю., Капустнік М.И., Диннік О.О.

ДІАГНОСТИЧНА РОЛЬ ЗМІН ПОКАЗНИКІВ МІСЦЕВОГО І СИСТЕМНОГО ІМУНІТЕТУ У ВАГІТНИХ ЖІНОК З БАКТЕРІАЛЬНОЮ ІНФЕКЦІЄЮ

Харківський національний медичний університет

У статті описується прогнозування неонатальних ускладнень на основі комплексного клінічного та імунологічного обстеження вагітних жінок. У дослідження були включені 35 вагітних жінок, які були розділені на дві групи. У першу групу (основну) були включені 25 пацієнтів з внутрышньоутробними ынфекцыями (ВУІ) у новонароджених в ранньому неонатальному періоді, у другу (контрольну) - 10 пацієнтів без реалізації ВУІ у новонароджених. Кількісне дослідження рівня прозапальних цитокінів в сироватці крові вагітної та вмісті заднього склепіння піхви показали значне збільшення IL-8 (16.73 пг / мл, р = 0,021) і IL - 6 (38,4 пг / мл, р = 0,032) у сироватці крові вагітних жінок р = 0,032), які народили дітей з ВУІ. Рівень цитокінів у вмісті заднього склепіння піхви також був збільшений в першій групі вагітних: IL-6 (89, 41 мг / г) та ІЛ-1в (157,2 г / г) (р <0,05). Отже результати дослідження з визначення імунологічних маркерів запалення дозволяють прогнозувати виникнення ранніх неонатальних ускладнень у вагітних, що знаходяться в групі ризику по розвитку ВУІ, що дозволяє знизити ризик інфекційних ускладнень у новонароджених шляхом проведення своєчасних профілактичних і лікувальних заходів.

Ключові слова: цитокіни, внутрішньоутробна інфекція, С-реактивний білок, імунологічні маркери.

РЕЗЮМЕ

Щербина И.М., Плахотная И.Ю., Капустник Н.И., Дынник О.О.

ДИАГНОСТИЧЕСКАЯ РОЛЬ ИЗМЕНЕНИЙ ПОКАЗАТЕЛЕЙ МЕСТНОГО И СИСТЕМНОГО ИММУНИТЕТА У БЕРЕМЕННЫХ ЖЕНЩИН С БАКТЕРИАЛЬНОЙ ИНФЕКЦИЕЙ

Харьковский национальный медицинский университет

В статье описывается прогнозирование неонатальных осложнений на основе комплексного клинического и иммунологического обследования беременных женщин. В исследование были включены 35 беременных женщин, которые были разделены на две группы. В первую группу (основную) были включены 25 пациентов с ВУИ у новорожденных в раннем неонатальном периоде, во вторую (контрольную) - 10 пациентов без реализации ВУИ у новорожденных. Количественное исследование уровня провоспалительных цитокинов в сыворотке крови беременной и содержимом заднего свода влагалища показали значительное увеличение IL-8 (16.73 пг / мл, р = 0,021) и IL - 6 (38,4 пг / мл, р = 0,032) в сыворотке крови беременных женщин р = 0,032), которые родили детей с ВУИ. Уровень цитокинов в содержимом заднего свода влагалища также был увеличен в первой группе беременных: IL-6 (89, 41 мг / г) и ИЛ-1в (157,2 г/г) (р <0,05). Результаты исследования по определению иммунологических маркеров воспаления позволяют прогнозировать возникновение ранних неонатальных осложнений у беременных, находящихся в группе риска по развитию ВУИ, что позволяет снизить риск инфекционных осложнений у новорожденных путем проведения своевременных профилактических и лечебных мероприятий.

Ключевые слова: цитокины, внутриутробная инфекция, С-реактивный белок, иммунологические маркеры.

Received: 27-Feb. – 2016
Accepted: 30-Mar. - 2016