ПЕДІАТРІЯ

УДК 616.24-002.17:616.899.65-053.36-07

M.O. Gonchar, Doctor of Med. Sc., Professor,
Head of the Department of Pediatrics № 1 and Neonatology,
O.L. Logvinova, Doktor of Med. Sc., associete professor,
O.P. Pomazunovska*, cand. of Med Sc., assistant of the Department,
Head of the Pediatric Department

Kharkiv National Medical University

****Kharkiv Regional Children's Hospital***

THE RISK FACTORS OF DEVELOPMENT OF THE INTERSTITIAL LUNG DISEASE IN CHILDREN WITH THE TRISOMY OF 21ST CHROMOSOME

The diagnosis an interstitial lung disease in children has a number of difficulties, even if you have results of high-tech methods of research. The article identifies the main risk factors for development of interstitial lung disease in children with trisomy of 21st chromosome. It is proved that the presence of a child combined heart defects, the use of extracorporeal circulation and prolonged artificial ventilation of the lungs during cardiac surgery, and the presence of adverse perinatal anamnesis have the greatest influence on the formation of interstitial lung disease in children with trisomy of 21st chromosome.

Keywords: *an interstitial lung disease, risk factors, children, a trisomy of 21st chromosome.*

In children's pulmonology the diagnosis an interstitial lung disease (ILD) is established seldom, even if presence results of a high-separate computer tomography and investigation of bronchoalveolar to lavage. Low level of diagnosis of ILD is determined by several factors. First: interstitial lung disease in children (chILD) in the majority of aspects considerably differ from ILD in adults. Frequency of supervision of ILD in children is 0.36/100 000, compared with 60–80/100 000 in adults [1]. Secondly, a range of nosological forms at children considerably higher than in adults, due to development and growth of lungs which continues after the birth [2]. Thirdly, 10 % of nosological forms in structure of chILD is malformation of alveoles and vessels, genetic defects of SpB and SpC proteins of surfactant and a gene of ABCA3 responsible for synthesis of corpuscles of lamilyarias [3, 4].

It is known that for children with a trisomy of 21st chromosome typical malformation of lungs which were already formed at the time of the birth: underdevelopment of alveoluses, misplaced of vessels and hypertrophy of muscular layer of arterioles. The last quite often unite to inborn heart defects [5–8]. However still unknown of features of growth of lungs in children with a trisomy of 21st chromosome in the postneonatal period, risk factors of development of chILD and pathomorphological changes at accession of comorbid pathology of respiratory and cardiovascular systems.

Purpose – improvement of diagnosis of an interstitial lung disease in children with a trisomy of 21st chromosome by determination and a clustering of risk factors of a disease.

Material and methods

The 37 children with a trisomy of 21st chromosome among which 14 (37.8 %) with chILD (the main group) and 23 (62.1 %) that was not created by chILD (group of comparison) were observed. Middle age of inspected children

of the main group was (9.7±2.4) months, group of comparison – (11.2±3.6) months (r>0.05). Examination of children was conducted from 2007 to 2016 at Department of Pediatrics № 1 and Neonatology of the Kharkiv National Medical University on the basis of Regional Children's Hospital.

Assessment of physical development at the birth, the analysis of obstetric, pre- and perinatal anamnesis, influence of comorbid pathology carried out at all children of the general population. Extracts from histories of development of the newborn and results of interview with the child's parents were sources of the anamnesis. The diagnosis an interstitial lung disease was established according to the criteria and the standard recommended by the American Thoracic Society in 2015 [9]. Existence of a cystic fibrosis, an agenesia, aplasia of a cystous hypoplasia of lungs, tracheobronchomegalies, a stenosis of a trachea, Williams–Campbell's syndrom, Kartagener's syndrom, inborn lobar emphysema, diverticulums of a trachea and bronchs, sequestration of lungs, a bronchoectatic disease, defects of heart and vessels were considered as criteries of an exception of patients from examination. Diagnosis of diseases which entered criteria of an exception of patients from research was carried out on the basis of orders MH of Ukraine of 13.01.05 № 18 «About the adoption of protocols of providing medical care to children behind the specialty Children's Pulmonology» and of 19.07.05 № 362 «About the adoption of protocols of diagnostic and treatment of cardiorheumatological diseases in children».

Investigation of a respiratory organs and heart is carried out by the standard program with included of methods palpation, percussion, auscultation. To evaluate pulmonary hemodynamics used a Doppler echocardiography. Statistical data was processed with use of the program STATISTICA-6.

Results and discussion

In the analysis of the obstetric anamnesis at a disease of respiratory system at mothers of children of the main group is (6.7±1.7) %: one mother has a chronic bronchitis, and another – bronchial asthma (table 1). Existence of a chronic disease of respiratory system in mother did not influence of the development of ILD in the child (DI 0.02–0.61; F(1,247)=0.27; p=0.603).

In I and III trimester of pregnancy mothers of children from both groups had an acute respiratory disease with the same frequency. In II trimester of pregnancy the acute respiratory disease was observed at 85.7 % mothers of the main group which was reliable more often (r<0,05). Influence of an acute respiratory disease in II trimester of pregnancy on formation of chILD was proved (DI 0.37–0.79; F(1.247)=3.93; p=0.049). II trimester of pregnancy is the period when are formed channels in a mesenchyma of lungs, development of terminal bronchioles and an acinus comes to end.

From pathology of pregnancy in mothers of children of the main group authentically more often were an oligohydramnios (r=0.046) and threat of abortion (r=0.024), table 2. More frequent formation of chILD depending on presence of multiple pregnancy it was not revealed (r>0.05). However, influence of combination of such factors: multiple pregnancy and EHMT/DNMT at the birth on formation of chILD was revealed (λ Wilks – 0.745; F(2.765)=8.456; p=0,001).

Table 1. Frequency of somatic and gynecological diseases at mothers of children of the main group and comparisons group

Diseases	The main group (n=14)		Group of comparison (n=23)		p
	abs.	% (M±m)	abs.	% (M±m)	
Diseases of respiratory system					
bronchial asthma	1	7.1±1.6	0	–	0.6780
chronic bronchitis	1	7.1±1.6	0	–	0.6480
Acute respiratory infection, in trimester of pregnancy					
I	1	7.1±1.6	1	4.3±3.2	0.8160
II	12	85.7±2.3	1	4.3±3.2	0.0491
III	1	7.1±1.6	1	4.3±3.2	0.5360

Notes: 1. Distinctions not reliable (X^0 – r>0.05).
2. Distinctions are reliable (X^1 – r<0.05).

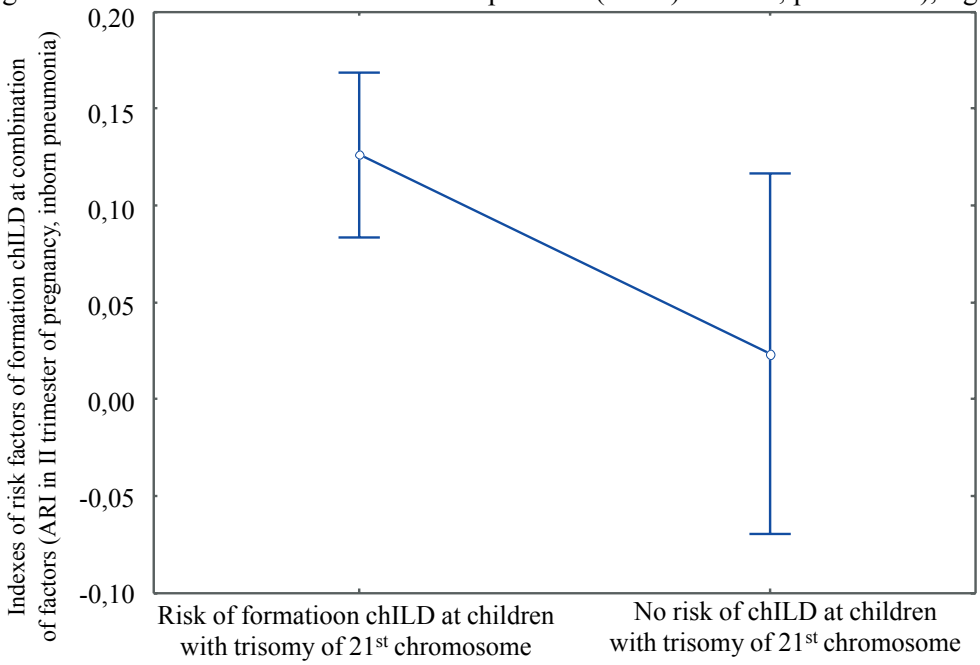
Table 2. Features of course of pregnancy in mothers of children of main group and group of comparison

Morbid conditions	Main group (n=14)		Group of comparison (n=23)		p
	abs.	% (M±m)	abs.	% (M±m)	
Gestosis					
early	6	42.8±3.0	10	43.5±2.5	0.7270
late	4	28.5±2.8	5	21.7±2.2	0.8210
Hypertension of pregnant women	7	50.0±2.4	9	39.1±3.9	0.5440
Gestational diabetes mellitus	2	14.3±2.4	0	–	0.5180
Anemia of pregnant women, degree					
mild	2	14.3±2.4	7	30.4±2.7	0.9030
moderately	9	64.3±1.9	4	17.4±2.5	0.9060
severe	0	–	0	–	
Threat of abortion	12	85.7±2.9	18	78.2±2.6	0.000084
Oligohydramnios	12	85.7±2.3	0	–	0.0461
Polihydramnios	4	28.5±2.8	2	8.7±2.2	0.2710
Multiple pregnancy	11	78.6±2.6	6	26.1±2.3	0.3850

Notes: 1. Distinctions not reliable (X^0 – r>0,05).
2. Distinctions are reliable (X^1 – r<0,05; X^4 – r<0,0001).

Mothers of children of the main group had class IgG AB to U. Urealyticum [7 mothers; (50.0±2.4) %], Cytomegalovirus [5 notices; (35.7±2.2) %]. At clinical examination, an immune-enzyme analysis of specific IgM and a polimeraz chain reaction the cytomegalovirus infection was revealed by at one child [(7.1± 2.4) %]. IgG to U. urealyticum and Cytomegalovirus at mothers of children of comparison group were not revealed. According to our re-search, the interrelation between chILD with a Cytomegalovirus infection was revealed (r=0.567; r<0.05).

The reliable interrelation of a combination of an acute respiratory infection in II trimester of pregnancy, prenatal pneumonia with formation of chILD was proved (λ Wilks – 0.885; F(3.245)=10.551; p=0.00001), figure.



Graphic results of influence on formation of chILD in children with trisomy of 21st chromosome at such combination of factors: acute respiratory infection in II trimester of pregnancy, threat of abortion

An inborn heart defects had 11 [(85.7± 2.9) %] children of the main group and 9 [(39.1± 3.9) %] patients from group of comparison (r<0.05), table 3. Children with trisomy of 21st chromosome who had chILD were had combined defects reliable more often: atrioventricular communication and transposition of the main vessels (r<0.05). At 9 [(64.3±1.9) %] children of the main group and 4 [(17.4±2.5) %] patients of group of comparison were carried out of cardiosurgical intervention with use of artificial ventilation of the lungs and the machine of artificial blood circulation (r<0.05).

An artificial ventilation of the lungs was longer in children of chILD with a trisomy of 21st chromosome: (11.5±2.13) days in the main group and (2.70±0.95) days in group of comparison (r<0.01). The influence of existence of the combined heart defects, long artificial ventilation of the lungs (>7 days) and use of the machine of artificial blood circulation during operation on development of chILD in children with a trisomy of 21st chromosome was revealed (to F (5.79)=16.8; p=0.002).

Table 3. Structure of inborn heart defects in main group and group of comparison

Inborn heart defect	Main group (n=14)		Group of comparison (n=23)		p
	abs.	% (M±m)	abs.	% (M±m)	
ASD	0	–	3	13.0±2.5	0.0011
VSD	3	21.4±2.9	4	17.4±2.5	0.2641
PDA	4	28.5±2.8	0	–	0.0011
Transposition of the main vessels	2	14.3±2.4	0	–	0.0011
Other combined heart defects with enrichment of a small circle of blood circulation	2	14.3±2.4	2	8.7±2.2	0.1110

Notes: 1. Distinctions not reliable (X^0 – r>0.05).
2. Distinctions are reliable (X^1 – r<0.05).

Conclusions

1. The maximum value in formation of chILD at children with a trisomy of 21st chromosome was existented in children with combined heart defects or other inborn heart defects with enrichment of a small circle of blood circulation, using of the machine of artificial blood circulation and long artificial ventilation of the lungs (>7 days) during cardiac operation.

2. In formation of chILD at children with a trisomy of 21st chromosome the adverse perinatal anamnesis (an acute respiratory infection at mother in II trimester of pregnancy, inborn pneumonia in a neonate) and a cytomegalovirus infection in the anamnesis of the child with a trisomy of 21st chromosome had smaller cluster value.

References

1. Childhood interstitial lung disease: a systematic review / N. J. Hime, Y. Zurynski, D. Fitzgerald [et al.] // Pediatr. Pulmonol. – 2015. – Vol. 50. – P. 1383–1392.

2. Classification, evaluation and management of childhood interstitial lung disease in infancy / G. Kurland, R. R. Deterding, J. S. Hagood [et al.] // Am. J. Respir. Crit. Care Med. – 2013. – Vol. 188. – P. 376–394.

3. Diffuse lung disease in young children: application of a novel classification scheme / G. H. Deutsch, L. R. Young, R. R. Deterding [et al.] // Am. J. Respir. Crit. Care Med. – 2007. – Vol. 176. – P. 1120–1128.

4. *Dinwiddie R.* Idiopathic interstitial pneumonitis in children: a national survey in the United Kingdom and Ireland / R. Dinwiddie, N. Sharief, O.Crawford // Pediatr. Pulmonol. – 2002. – Vol. 34. – P. 23–29.

5. Incidence and classification of pediatric diffuse parenchymal lung diseases in Germany / M. Griese, M. Haug, F. Brasch [et al.] // Orphanet. J. Rare Dis. – 2009. – Vol. 4. – P. 26.

6. The incidence of interstitial lung disease 1995–2005: a Danish nationwide population-based study / J. B. Kornum, S. Christensen, M. Grijota [et al.] // BMC Pulm. Med. – 2008. – Vol. 8. – P. 24.

7. *Clement A.* ERS Task Force. Task Force on chronic interstitial lung disease in immunocompetent children / A. Clement // Eur. Respir. J. – 2004. – Vol. 24. – P. 686–697.

8. Interstitial lung diseases in children / A. Clement, N. Nathan, R. Epaud [et al.] // Orphanet. J. Rare Dis. – 2010. – Vol. 5. – P. 22.

9. A national internet-linked based database for pediatric interstitial lung diseases: the French network / N. Nathan, R. A. Taam, R. Epaud [et al.] // Orphanet. Journal of Rare Diseases. – 2012. – Vol. 7. – P. 40.

М.О. Гончарь, О.Л. Логвінова, О.П. Помазуновська

ФАКТОРИ РИЗИКУ РОЗВИТКУ ІНТЕРСТИЦІЙНОЇ ХВОРОБИ ЛЕГЕНЬ У ДІТЕЙ З ТРИСОМІЄЮ ЗА 21-ю ХРОМОСОМОЮ

Встановлення діагнозу інтерстиційна хвороба легень у дітей має ряд складностей навіть за наявності результатів дослідження високотехнологічними методами. У статті вказано основні фактори ризику розвитку інтерстиційної хвороби легень у дітей з трисомією за 21-ю хромосомою. Доведено, що наявність у дитини комбінованої вади серця, використання апарату штучного кровообігу та тривалої штучної вентиляції легень під час кардіохірургічної операції, а також наявність несприятливого перинатального анамнезу чинять найбільший вплив на формування інтерстиційного захворювання легень у дітей з трисомією за 21-ю хромосомою.

Ключові слова: *інтерстиційна хвороба легень, фактори ризику, діти, трисомія за 21-ю хромосомою*.

М.А. Гончарь, О.Л. Логвинова, Е.П. Помазуновская

ФАКТОРЫ РИСКА РАЗВИТИЯ ИНТЕРСТИЦИАЛЬНОЙ БОЛЕЗНИ ЛЕГКИХ У ДЕТЕЙ С ТРИСОМИЕЙ ПО 21-Й ХРОМОСОМЕ

Установление диагноза интерстициальной болезни легких у детей имеет ряд сложностей даже при имеющихся результатах исследования высокотехнологичными методами. В статье указаны основные факторы риска развития интерстициальной болезни легких у детей с трисомией по 21-й хромосоме. Доказано, что наличие у ребенка комбинированного порока сердца, использование аппарата искусственного кровообращения и длительной искусственной вентиляции легких во время кардиохирургической операции, а также наличие неблагоприятного перинатального анамнеза оказывают наибольшее влияние на формирование интерстициальной болезни легких у детей с трисомией по 21-й хромосоме.

Ключевые слова: *интерстициальная болезнь легких, факторы риска, дети, трисомия по 21-й хромосоме.*

Надійшла до редакції 13.03.17