ANALYSIS OF CAUSATIVE FACTORS OF RECURRENT BRONCHIAL OBSTRUCTION SYNDROME IN YOUNG CHILDREN

[1,5]Matsyura O., [1,5]Besh L., [2]Zubchenko S., [3]Zaremba N., [4]Slaba O.

Danylo Halytsky Lviv National Medical University, [1]Department of Pediatrics №2, [2]Department of Clinical Immunology and Allergology, [3]Department of Social Medicine, Economics and Organization of Health Care, [4]Department of Internal Medicine №2; [5]Communal Nonprofit Enterprise "City Children's Clinical Hospital of Lviv", Ukraine

Currently, there is the tendency in the world to increase in the number of miscarriages, increase in the number of premature babies; thus, the issue of providing complete medical aid to such children is topical [4]. Newborns that for different reasons required prolonged respiratory maintenance – artificial ventilation (AV), spontaneous breathing with continuous positive airway pressure (SBCPAP), oxygen therapy, are more frequently surviving nowadays. Simultaneously, increased number of complications is observed on the background of positive clinical effects of administering certain component of intensive therapy [1,5].

Bronchopulmonary obstruction is one of the most severe complications of the syndrome of respiratory disorders, AV with high concentrations of oxygen in premature children [3]. A topical issue is the search for the factors, which cause appearance of recurrent bronchial obstruction syndrome, since knowledge of causes is an important component and background for prophylaxis [2].

The aim of the work was to conduct analysis of factors causing appearance of recurrent bronchial obstruction syndrome.

Material and methods. Analysis of 485 case histories of children, who were treated in Communal Nonprofit Enterprise "City Children's Clinical Hospital of Lviv", was conducted. Anamnestic data were recorded in a specially designed questionnaire. For further study of children's health under 3 years of age, 420 questionnaires were sent, which enabled to obtain information from parents. Thus, 231 questionnaires were studied thoroughly.

Ethical Committee or Institutional Animal Care and Use Committee Approval: Danylo Halytsky Lviv National Medical University 20/12/2010 № 10; Nonprofit Communal Enterprise "City Children's Clinical Hospital of Lviv"; 16.Nov.2018 № 6.

Results and discussion. We analyzed the role of 77 factors, calculating coefficients of correlation with the formation of recurrent bronchial obstruction syndrome for each of them. Conducted statistical analysis enables to isolate 24 signs among these factors, which significantly correlated with the formation of recurrent BOS in young children, in particular:
- Respiratory therapy in neonatal period (A);
- Respiratory disorders in neonatal period (B);
- Gestational age ≤ 36 weeks (C);
- Weight at birth <1500 g (D);
- Unfavorable ecology of living conditions (E);
- Threatened termination of a particular pregnancy (in II half) (F);
- Severe gestosis (in II half) (G);
- Cesarean section (H);
- Prolonged period without amniotic fluid (I);
- Allergy in a child (J);
- Bronchial asthma in parents (K);
- Allergy in a mother (L);
- Nonspecific lung diseases in relatives (M);
- Mother's smoking during pregnancy (N);
- Passive smoking (O);
- Early artificial feeding (P);
- Administration of surfactant (Q);
- Frequent acute respiratory infections (R);
- Apgar score at 5 minute (S);

- Conduction of antibacterial therapy for a mother during pregnancy (T);
- Conduction of histogenous maintaining therapy (U);
- Pathological course of pregnancy and delivery (V);
- Extragenital pathology in a mother (W);
- Inflammatory diseases in a mother during pregnancy (X).

For each of the aforementioned factors, coefficients of correlation with the development of recurrent bronchial obstruction syndrome were calculated and are presented in Table 1.

Fig. 1 presents dependence between gestational age, total period of respiratory therapy and probability of development of recurrent bronchial obstruction syndrome.

This figure presents that the highest risk of recurrent bronchial obstruction syndrome development in children born before 29 gestational week with simultaneous combination of prolonged (over 700 hours) total period of respiratory therapy.

Presence of respiratory therapy significantly determines the risk of appearance of recurrent bronchial obstruction syndrome in children, who did not undergo respiratory therapy, thus, the risk of appearance of such pathology is commonly low. Simultaneously with the increase in duration of respiratory therapy, the risk increases, however, further it also depends on gestational age. Analyzed data indicate that the lowest risk exists in the group of children who were over 36 weeks and did not undergo respiratory therapy. Simultaneously with the increase in gestational age, the risk of appearance of this disease decreases.

The results of our investigations enable to state that the development of bronchial obstruction syndrome in children could be prevented, having distinct criteria for calculation of this pathology development.

Literature data on prognosis of recurrent bronchial obstruction syndrome in children, who suffered respiratory disorders in neonatal period, are single and usually restricted to a record of certain unfavorable factors, which cause the development of this pathology [2, 6]. There are some papers dedicated to calculation of risk factors of recurrent bronchial obstruction syndrome in young children, however, we did not find the works, which would allow conduction of individual analysis of risk factors of the disease development in the children with respiratory disorders in neonatal period.

Based on the aforementioned facts, there is the need in elaboration of the method of individual calculation of the risk of recurrent bronchial obstruction syndrome development in young children, who had respiratory disorders in neonatal period [6].

To compile a mathematical model of bronchial obstruction syndrome development in young children with respiratory disorders in neonatal period, a logistic regression method was applied. Logistic regression analysis enables to build a mathematical model for prognosis of events probability based on present data (independent signs). A dependent sign of Y, as opposite to linear multiple regression, is not the value P, but its logit transformation. Logit transformation enables, instead of P values determined at interval [0; 1], to transform to interval [$-\infty$; $+\infty$]. Thus, the sensitivity of this function to changes in combinations of different prognostic signs increases.

*Table 1. Correlative connection of some factors with the development
of recurrent bronchial obstruction syndrome in young children*

| Factor		R	P
Respiratory therapy in neonatal period	A	0.53	< 0.01
Respiratory disorders in neonatal period	B	0.28	< 0.01
Gestational age ≤ 36 weeks	C	0.28	< 0.01
Weight at birth <1500	D	0.23	< 0.01
Unfavorable ecology of living conditions	E	0.37	< 0.01
Threatened termination of the pregnancy (in II half)	F	0.21	< 0.01
Severe gestosis (in II half)	G	0.37	< 0.01
Cesarean section	H	0.28	< 0.01
Prolonged period without amniotic fluid	I	0.36	< 0.01
Child's allergy	J	0.32	< 0.01
BA in parents	K	0.46	< 0.01
Mother's allergy	L	0.36	< 0.01
Non-specific diseases of lungs in relatives	M	0.14	< 0.05
Mother's smoking during pregnancy	N	0.48	< 0.01
Passive smoking	O	0.30	< 0.01
Early artificial feeding	P	0.44	< 0.01
Administration of surfactant	Q	-0.16	< 0.05
Frequent acute respiratory infections in a child	R	0.44	< 0.01
Apgar score at 5 min ≤ 6 points	S	0.39	< 0.01
Conduction of antibacterial therapy	T	0.15	< 0.01
Conduction of histogenous maintaining therapy	U	0.22	< 0.01
Pathological course of pregnancy and delivery	V	0.41	< 0.01
Extragenital pathology in a mother	W	0.33	< 0.01
Inflammatory diseases in a mother during pregnancy	X	0.22	< 0.01
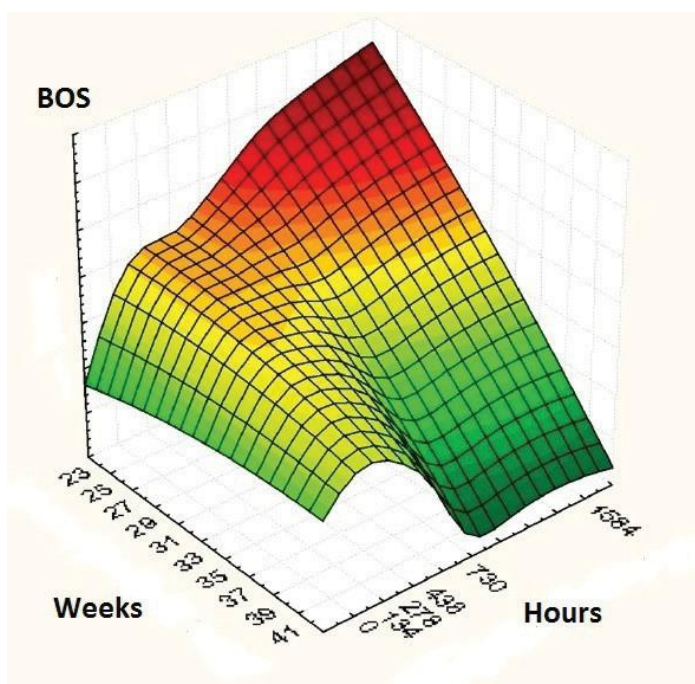
*Fig. 1. Dependence between gestational age, total period of respiratory therapy
in neonatal period and probability of development of bronchial obstruction diseases*

Table 2. Assessment results of investigations by logistic regression method

№		Factors	Regression coefficient (β_n)
		Constant β_0	**-5.211**
1	A	Respiratory therapy in neonatal period	0.11
2	C	Gestational age $\leq$ 36 weeks	1.592
3	N	Mother's smoking during pregnancy	2.052
4	Q	Introduction of surfactant	-1.705
5	S	Apgar score at 5 min $\leq$ 6 point	0.912

Table 3. Probability of appearance of recurrent bronchial obstruction syndrome in young children

B_1 Respiratory therapy	B_2 Gestational age < 36 weeks	B_3 Mother's smoking during pregnancy	B_4 Administration of surfactant	B_5 Apgar score at 5 min $\leq$ 6 points	P
A	C	N	Q	S	
1	2	3	4	5	6
0	0	0	0	0	0.005427
0	0	0	0	1	0.013400
0	0	0	1	0	0.000991
0	0	0	1	1	0.002463
0	0	1	0	0	0.040738
0	0	1	0	1	0.095609
0	0	1	1	0	0.007660
0	0	1	1	1	0.018854
0	1	0	0	0	0.026110
0	1	0	0	1	0.062562
0	1	0	1	0	0.004850
0	1	0	1	1	0.011986
0	1	1	0	0	0.172645
0	1	1	0	1	0.341864
0	1	1	1	0	0.036544
0	1	1	1	1	0.086274
1	0	0	0	0	0.006054
1	0	0	0	1	0.014935
1	0	0	1	0	0.001106
1	0	0	1	1	0.002748
1	0	1	0	0	0.045261
1	0	1	0	1	0.105552
1	0	1	1	0	0.008544
1	0	1	1	1	0.021000
1	1	0	0	0	0.029057
1	1	0	0	1	0.069332
1	1	0	1	0	0.005410
1	1	0	1	1	0.013361
1	1	1	0	0	0.188927
1	1	1	0	1	0.367025
1	1	1	1	0	0.040621
1	1	1	1	1	0.095350

This method allows detecting dependence of the sign investigated (formation of recurrent bronchial obstruction syndrome) simultaneously on several other signs and making appropriate prognosis [7].

The methods of such profound modern statistical analysis enabled us to choose, among a complex of interconnected factors, that influence the formation of recurrent bronchial obstructive syndrome in children, five signs, which had the highest statistically reliable influence, namely, increased the risk: respiratory therapy in neonatal period (A), gestational age ≤ 36 weeks (C); mother's smoking during pregnancy (N); Apgar score at 5 min ≤ 6 points (S), and decreased the risk – administration of surfactant (Q). These factors were included in prognostic mathematical model. Results of analysis using logistic regression method are presented in Table 2.

Probability (p) of calculated coefficients constitutes 0.00001.

Probability of development of recurrent bronchial obstruction syndrome depending on chosen factors has been calculated by formula 1:

$$P = e^y/(1+e^y) \text{ (1)},$$

where e = 2,71828…. – basis of natural logarithms,

Y – value calculated by formula 2:

$$Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \ldots \beta_n X_n, \text{ (2)},$$

where β_0 – constant,

β_n – coefficient in each factor,

X_n – value of factors.

Having put the results in formula, we received Y value for prognosis of bronchial obstruction syndrome development:

$$Y = -5.211 + 0.11*A + 1.592*C + 2.052*N - 1.705*Q + 0.912*S \text{ (3)}$$

The oretically *p* can assume value from 0 (impossible event) to 1 (event always occurs).

For convenience of practical use of the obtained results, probabilities of appearance of recurrent bronchial obstruction syndrome in young children depending on various combinations of risk factors were calculated and presented in table (Table 3). Every practical doctor can use such tables for individual calculation of the risk of recurrent bronchial obstruction syndrome development in young children.

As an illustrative example, we present the data of our monitoring. Girl A., 9 months of age, was born in I pregnancy, I delivery at gestational period 32 weeks (C=1) with body weight 1860 g. The course of pregnancy was without peculiarities. Amniotic membranes ruptured prematurely, period without amniotic fluid lasted 6 hours. Delivery was via natural birth canal. Assessment by Apgar score at the 1st and 5th minutes was 6 and 7 points, respectively (S=0). In 4 hours after birth, respiratory disorders were observed in the girl and respiratory distress syndrome was diagnosed. Due to intensification of respiratory disorders, the child was intubated and artificial ventilation was commenced (A=1). In 12 hours, the girl was transported from maternity unit to intensive care unit for neonates for further treatment. The patient was not administered surfactant into the trachea (Q = 0). Total period of respiratory therapy constituted 180 hours (artificial respiration – 18 hours, spontaneous breathing with continuous positive airway pressure – 148 hours, oxygen therapy – 14 hours). From the 3rd day of life, the child was on breastfeeding. Family anamnesis was not burdened. The family was complete, living conditions – satisfactory. During pregnancy the mother smoked 1-2 cigarettes a day (N=1).

Thus, conducted investigations enabled not only to detect the factors, which influence the development of bronchial obstruction syndrome in children, but also to suggest mathematical model of individual calculation of risk factors in this pathology. Data of conduction of mathematical analysis can be used for elaboration of a complex of rehabilitation measures concerning the development of recurrent bronchial obstruction syndrome in children, who suffered respiratory disorders in neonatal period.

Conclusions. 1. The presence of respiratory therapy in anamnesis, especially artificial ventilation significantly indicates the risk of recurrent bronchial obstruction syndrome development.

2. The highest risk of recurrent bronchial obstruction syndrome development exists in children born before 29 gestational week with simultaneous combination of prolonged (over 700 hours) total period of respiratory therapy.

3. The method of individual calculation of the risk of recurrent bronchial obstruction syndrome development in young children, who suffered respiratory disorders in neonatal period, has practical importance and can be used in everyday clinical practice.

REFERENCES

1. Bhandari V., Finer N.N., Ehrenkranz R.A. et al. Synchronized nasal intermittent positive pressure ventilation and neo natal outcomes: a retrospective study. Pediatrics 2009;124: 517–526.
2. Besh L., Matsyura O., Lishchuk-Yakymovych H. et al. Difficulties in differential diagnosis of skin allergies in children. Advanced Studies in Medical Sciences. – 2019. – Vol. 7, no. 1. – P. 1-10. https://doi.org/10.12988/asms.2019.912.
3. Committee on Fetus and Newborn. Respiratory support in preterm infants at birth. Pediatrics. 2014;133:171–174.
4. Force A. D. Acute respiratory distress syndrome. JAMA. 2012; 307, 2526–2533.
5. Isayama T, Chai-Adisaksopha C, McDonald SD. Noninvasive ventilation with vs without early surfactant to prevent chronic lung disease in preterm infants: a systematic review and meta-analysis. JAMA Pediatr. 2015;169:731–739.
6. Menshykova A.O., Dobryanskyy D.O., Salabay Z.V. et al. Choosing the type of respiratory support for preterm infants after extubation: noninvasive ventilation versus continuous positive airway pressure. Sovremennaya pediatriya.2016. 4(76): 91-96; doi10.15574/SP.2016.76.91.
7. Rabi Y, Soraisham A, et al. Outcomes of preterm infants following the introduction of room air resuscitation. 2015, 96: 252-259.

SUMMARY

ANALYSIS OF CAUSATIVE FACTORS OF RECURRENT BRONCHIAL OBSTRUCTION SYNDROME IN YOUNG CHILDREN

[1,5]**Matsyura O.**, [1,5]**Besh L.**, [2]**Zubchenko S.**, [3]**Zaremba N.**, [4]**Slaba O.**

Danylo Halytsky Lviv National Medical University, [1]Department of Pediatrics №2, [2]Department of Clinical Immunology and Allergology, [3]Department of Social Medicine, Economics and Organization of Health Care, [4]Department of Internal Medicine №2; [5]Communal Non-profit Enterprise "City Children's Clinical Hospital of Lviv", Ukraine

Nowadays, newborns that required prolonged respiratory maintenance for different reasons are more often surviving. In-

crease in the number of complications is observed on the background of positive clinical effects of certain component of intensive therapy. Search for the factors, which provoke appearance of recurrent bronchial obstruction syndrome, is an important component and basis of prophylaxis.

The aim of our research was to conduct analysis of factors that provoke the development of recurrent bronchial obstruction syndrome.

To build mathematical model of bronchial obstruction development in young children with respiratory disorders in neonatal period, the method of logistic regression was used.

The results of conducted analysis enabled to detect that the presence of respiratory therapy significantly determines the risk of appearance of recurrent bronchial obstruction syndrome and suggest mathematical model of individual calculation of risk factors in this pathology. Data of conduction of mathematical analysis can be used for elaboration of a complex of rehabilitation measures concerning the development of recurrent bronchial obstruction syndrome in children, who suffered respiratory disorders in neonatal period. The highest risk of recurrent bronchial obstruction syndrome development in children born before 29 gestational week with simultaneous combination of prolonged (over 700 hours) total period of respiratory therapy.

Elaborated method of individual calculation of the risk of recurrent bronchial obstruction syndrome development in young children, who experienced respiratory disorders in neonatal period, has practical significance and can be applied in everyday clinical practice.

Keywords: bronchial obstruction syndrome, respiratory disorders, neonatal period, young children, prognosis, risk of the disease development.

РЕЗЮМЕ

ФАКТОРЫ РИСКА, СПОСОБСТВУЮЩИЕ РАЗВИТИЮ СИНДРОМА РЕЗУЛЬТАТИВНОЙ БРОНХИАЛЬНОЙ ОБСТРУКЦИИ У ДЕТЕЙ

[1,5]Мацюра О.И, [1,5]Беш Л.В., [2]Зубченко С.А.,
[3]Заремба Н.И., [4]Слаба О.Р.

Львовский национальный медицинский университет им. д. галицкого, [1]кафедра педиатрии №2, [2]кафедра клинической иммунологии и аллергологии, [3]кафедра социальной медицины, экономики и организации здравоохранения, [4]кафедра внутренней медицины №2; [5]кнП "городская детская клиническая больница города Львова"; украина

Цель исследования - анализ факторов риска, обусловливающих возникновение рецидивирующего бронхообструктивного синдрома у детей.

Проведен анализ 485 историй болезни детей, лечившихся в КОО «Городская детская клиническая больница г. Львова». Анамнестические данные записывались в специально разработанную анкету. Для дальнейшего изучения здоровья детей в возрасте до 3 лет было отправлено 420 анкет, для получения информации от родителей, изучена 231 анкета.

Для построения математической модели развития бронхиальной обструкции у детей раннего возраста с дыхательными расстройствами в неонатальном периоде применен метод логистической регрессии.

Результаты проведенного анализа позволили установить, что наличие респираторной терапии существенно определяет риск появления рецидивирующего бронхообструтивного синдрома и предложить математическую модель индивидуального расчета факторов риска при этой патологии. Данные математического анализа могут быть использованы для разработки комплекса реабилитационных мероприятий при развитии синдрома рецидивирующей бронхиальной обструкции у детей, перенесших респираторные заболевания в неонатальном периоде. Наиболее высокий риск развития синдрома рецидивирующей бронхиальной обструкции наблюдается у детей, рожденных до 29 гестационной недели, при одновременном сочетании длительного (более 700 часов) общего периода респираторной терапии.

Разработанный способ индивидуального расчета риска развития рецидивирующего бронхообструктивного синдрома у детей раннего возраста с расстройствами дыхания в неонатальном периоде имеет практическое значение и может быть использован в повседневной клинической практике.

reziume

produqciuli bronquli obstruqciis sindromis ganviTarebis xelSemwyobi riskis faqtorebi bavSvebSi

[1,5]o.maciura, [1,5]l.beSi, [2]s.zubCenko, [3]n.zaremba, [4]o.slaba

lvovis d.galickis sax. erovnuli samedicino universiteti, [1]pediatriis #2 kaTedra, [2]imunologiisa da alergologiis kaTedra, [3]socialuri medicinis, ekonomikis da jandacvis organizaciis kaTedra, [4]Sinagani medicinis #2 kaTedra; [5]lvovis saqalaqo klinikuri saavadmyofo, ukraina

kvlevis mizans warmoadgenda bavSvebSi morecidive bronqoobstruqciuli sindromis ganviTarebis ganmapirobebeli riskis faqtorebis analizi.

Catarebulia bavSvebis 485 istoriis analizi, romlebic mkurnalobdnen lvovis saqalaqo klinikur saavadmyofoSi. anamnezuri monacemebi aRiricxeboda specialurad SemuSavebul anketaSi. 3 wlamde asakis bavSvebis janmrTelobis Semdgomi SeswavlisaTvis gagzavnili iyo 420 anketa, romelTa saSualebiTac informacia miRebul iqna mSoblebidan, Seswavlilia 231 anketa. neonatalur periodSi sunTqviTi darRvevebis mqone adreuli asakis bavSvebSi bronquli obstruqciis ganviTarebis maTematikuri modelis agebisaTvis gamoyenebuli iyo logistikuri regresiis meTodi.

Catarebuli analizis Sedegebma mixedviT dadgenilia, rom respiraciuli Terapiis arseboba arsebiTad gansazRvravs morecidive bronqoobstruqciuli sindromis ganviTarebis risks da iZleva riskis faqtorebis individuri gamoTvlis maTematikuri modelis SemuSavebis saSualebas am paTologiis dros. maTematikuri analizis monacemebi SeiZleba gamoyenebuli iyos reabilitaciuri RonisZiebebis kompleqsis SemuSavebisaTvis morecidive bronqoobstruqciuli sindromis ganviTarebis dros bavSvebSi, romlebmac gadaitanes

respiraciuli daavadebebi neonatalur period-Si. morecidive bronqoobstruqciuli sindromis ganviTarebis yvelaze maRali riski aRiniSna 29 gestaciur kviramde dabadebul bavSvebSi, amavdroulad xangrZlivi (700 saaTze meti) saerTo respiraciuli Terapiis arsebobis pirobebSi.

neonatalur periodSi sunTqviTi darRvevebis mqone adreuli asakis bavSvebSi morecidive bronqoobstruqciuli sindromis ganviTarebis riskis individuri gamoTvlis SemuSavebul meTods aqvs praqtikuli mniSvneloba da SeiZleba gamo-yenebuli iyos klinikur praqtikaSi.