

FORECASTING THE RISK OF OTHER RESPIRATORY DISORDERS AND THEIR COMPLICATIONS IN THE NEWBORNS

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✓ Resume,

According to the International Classification of Diseases X Revision (ICD X), respiratory disorders in newborns belong to class XVI, separate states of the perinatal period (included in one heading: "respiratory and cardiovascular disorders characteristic of the perinatal period"). Up to now, there have been different interpretations of concepts between domestic clinicians: respiratory distress, respiratory distress syndrome of the newborn (RDSN), respiratory distress syndrome.

Key words: Respiratory disorders, complications, newborn, prediction.

ЧАҚАЛОҚЛАРДА НАФАС ОЛИШ ТИЗИМИ БУЗИЛИШЛАРИ ВА УЛАРНИНГ АСОРАТЛАРИНИ КЕЛИБ ЧИҚИШ САБАБЛАРИНИ ПРОГНОЗЛАШ

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*Касалликларни халқаро таснифнинг 10 қайта қўриб чиқилиши (КХТ X) нафас олиш тизими касалликлари ва улардаги бузилишлар XVI синфга киритилган бўлиб, бунда перинатал давринг алоҳида ҳолати (битта бўлимида: ("нафас ва юрак қон-томир бузилишлари перинатал давр учун характерлидир дея айтиб ўтилган"). Бизгача шу соҳада ишлаган ва ҳозирги клиник амалиёт шифокорлари қуйидаги тушунчани шарҳлаган: респиратор дистресс, чақалоқлар респиратор дистресс*синдроми нафас бузилиши синдроми.*

Калит сўзлар: Нафас бузилишлари, асорат, чақалоқ, прогнозлаш.

ПРОГНОЗИРОВАНИЕ РИСКА ВОЗНИКНОВЕНИЯ ДЫХАТЕЛЬНЫХ РАССТРОЙСТВ И ИХ ОСЛОЖНЕНИЙ У НОВОРОЖДЕННЫХ

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Дыхательные расстройства у новорожденных по Международной классификации болезней X пересмотра (МКБ X) относятся к классу XVI отдельные состояния перинатального периода (включены в одну рубрику: ("дыхательные и сердечно-сосудистые нарушения, характерные для перинатального периода"). Между отечественными клиницистами вплоть до настоящего времени существовали разные толкования понятий: респираторный дистресс, респираторный дистресс-синдром новорожденных, синдром дыхательных расстройств.

Ключевые слова: Дыхательная расстройства, осложнения, новорожденный, прогнозирования.

Introduction

A method for predicting the development of respiratory disorders in newborns in the first hours of life is characterized by the fact that in newborns during the first 2 hours after birth, the state of the central link in the regulation of respiration and the condition of the ventilation-perfusion relationship in the lungs is evaluated, and the state of the central link in the regulation of respiration is estimated by capnographic form the curve, while in the presence of a capnographic curve, in more than 60% of which there is no alveolar plateau, the development of a disturbance of the central At this level, 60-80% predict the development of a mild degree of central regulation of respiratory regulation, with a value of 81-90%, predict the development of a moderate state of respiratory regulation, and if more than 90% predict development severe violation of the state of the central link in the regulation of respiration, and the state of the

ventilation-perfusion relations in the lungs is assessed by the concentration of CO₂ in the final portion of exhaled air and When this index value less than 3.2 vol. % in full-term infants and less than 3.0% by volume in premature infants predict the development of a combined violation of the ventilation and perfusion components of the ventilation-perfusion relations in the lungs, with a value of 3.3-4.0 vol. % in full-term and 3.1-3.6% by volume in premature infants predict the development of a violation of the perfusion component of the ventilation-perfusion relationship in the lungs, with a value of 4.1-4.8% by volume in full-term and 3.7-4, 4% by volume in premature babies predict the development of a normal state of ventilation-perfusion relations in the lungs, and with a value of more than 4.8% by volume in full-term and more than 4.4% by volume. % in premature babies predict the development of a violation of the ventilation component of the ventilation-perfusion relationship in the lungs. The method provides greater reliability and accuracy.



Respiratory disorders (DR), or respiratory distress (from the English. Respiratory distress - respiratory disorders) - the presence of signs of respiratory failure (DN) in a newborn. Respiratory disorders are characterized by the following clinical features: cyanosis, tachypnea, swelling of the wings of the nose, difficulty breathing out, retraction of pliant areas of the chest, noisy breathing out. If a newborn has two or more clinical signs out of four, they say, then they say that he has respiratory distress [2,5,9].

Respiratory disorders rank first among the causes of early neonatal mortality (35.3%) and are one of the leading causes of perinatal mortality (16.3%) [1,2,7]. In surviving children, there is a significant increase in the likelihood of developing acute and chronic diseases and various neurological disorders in subsequent age periods [4,8,12]. Of greatest interest are pneumonia and respiratory distress syndrome of the newborn (RDSN), which is due to their predominance in the structure of the respiratory disorders of the perinatal period. Different outcomes in comparable in many indicators of newborns suggest the influence of genetic risk factors on the development of respiratory failure (DN) [3,7,11]. Considering pathogenesis, polymorphic variants of SFTPB, IL-1B, IL-1RN, IL-10, TNF-a, LTA, ACE genes can play an important role in the outcome of respiratory disorders, since they determine the balance between surfactant and cytokines.

Infections of the perinatal period and sepsis are not uncommon complications in newborns with respiratory disorders. The criteria for sepsis used in practice are not specific enough, as a result of which methods for predicting the infectious process in newborns have not become widespread in general clinical practice. In the light of modern concepts of sepsis, we believe that polymorphic variants of cytokine and angiotensin-converting enzyme (ACE) genes can affect the development of septic complications in newborns with respiratory disorders. Since the presence of a single risk factor may not always be the cause of a particular disease, forecasting, combining anamnestic, clinical and genetic risk factors in our opinion, is of practical importance, since it will allow for the correction of treatment of diseases.

Purpose of the study

Conduct a comprehensive assessment of risk factors to develop criteria for predicting the development of respiratory disorders and their infectious complications in newborns.

Materials and research methods

To perform the tasks of the study, two samples of newborns were formed. Full-term patients (n = 127) are represented by subgroups of healthy children without respiratory disorders - "control 1" (n = 100) and patients with pneumonia - "patients 1" (n = 27). The group of premature patients (n = 81) is represented by premature without respiratory disorders - "control 2" (n ~ 27) and patients with respiratory distress syndrome of the newborn - "patients 2" (n = 54). Criteria for inclusion in subgroups "patients 1" and "patients 2": the presence of severe DN from the first hours of birth, which required respiratory therapy, treatment in conditions of resuscitation of newborns. Exclusion criteria: congenital malformations of development, malformations of the central nervous system.

The control group "control 1" includes practically healthy full-term newborns without respiratory disorders, who were discharged from the maternity hospital on the 4-5th day of life.

The results of the study. As a result of the research, the following facts were established. Of the clinical parameters, asphyxia is a significant factor for the development of pneumonia in term infants. The Apgar score up to 7 on the 5th minute of life had a statistically significant difference (24% in "control 1" versus 97% in "patients 1", $p = 0.001$) and was a risk factor for the development of pneumonia: OR = 82.33; 95% CI 11.82 - 1685.03. In addition, these indicators are established as risk factors for the development of pneumonia in full-term newborns.

Note that birth asphyxia is the most important prognostic sign of pneumonia. Gestational age in the subgroup of patients with pneumonia tends to decrease to 37-38 weeks. The age interval of mothers in patients with pneumonia is characterized by such extreme points as 16 years and over 36 years. The latter confirms the influence of the biological age of the mother on the development of diseases in newborns. Mass at birth as a criterion for the health of the child also confirmed its significance for the prediction, since it can be seen that this parameter in newborns with pneumonia is at the extreme limit of the norm for full-term children (in the range 2353-2594). A long anhydrous period (more than 24 hours) is also a risk factor for the development of pneumonia. The need for respiratory therapy immediately after birth, associated with asphyxia, leads to a secondary deficiency of surfactant and lung damage. Therefore, it logically serves as a prognostic sign of the development of pneumonia in newborns.

Analysis of risk factors in the group of premature babies demonstrated the absence of a statistically significant difference in the overwhelming majority of social, demographic, ante- and intranatal, clinical and anthropometric indicators. The risk factors for RDSN are HFPN ($p = 0.023$) and acute inflammatory diseases in a pregnant woman ($p = 0.001$).

On the distribution of polymorphic variants of genes: 11-1 V, K-1Sh, I-10, ShG-a, ACE - premature newborns were not statistically significant BRTRV among subgroups of premature received the following results.

Гомозиготный генотип СС выявлен у 30,77% пациентов в подгруппе "больные 2" против 12,00% в "контроле 2" ($p > 0.05$). Гетерозиготный генотип СТ практически с одинаковой частотой встречался как у больных недоношенных (50,0%), так и у недоношенных без дыхательных расстройств (48,0%), $p > 0.05$. Генотип ТТ изучаемого полиморфного локуса в два раза чаще встречался у недоношенных в "контроле 2": 40,00% против 19,23% в подгруппе "больные 2", различия приближались к статистически значимым ($p = 0.05$). Аллель Т статистически значимо преобладал у недоношенных новорожденных в "контроле 2" (64,0% против 44,23% в подгруппе "больные 2", $\chi^2 = 5.280$, $< 1\% = 1$, $p = 0.02$, СЖ = 0.45). Аллель С статистически значимо преобладал у больных РДСН (55,77% против 36,00% в подгруппе "контроль 1", $\chi^2 = 5.28$, ϵ_m (Ж = 2.24, 95% СІ 1.06-4.80) и является фактором повышенного риска респираторного дистресс-синдрома новорожденных (табл.5). Таким образом, полиморфные варианты гена БРТРВ являются важнейшими детерминантами респираторного дистресс-синдрома новорожденных.

Haataja R., (2002), Hallman M., (2002) found no statistically significant differences in the frequency distribution of the polymorphic variants of the SFTPB gene among rdsH patients and healthy newborns. Floros J. et al. (2001) found that changes in the intron 4 of the SFTPB gene are a risk factor for the formation of RDSH for the female Negroid race. R.R. Lyra (2007), when studying the same polymorphism, comparing preterm with RDSH with healthy full-term newborns, did not find significant differences. Polymorphic locus 1580C> T exon 4 SFTPB, which is responsible for replacing the amino acid isoleucine with threonine at position 131, was investigated by Lin Z. et al. (2000), Marttila R. (2003). It was established that the T (isoleucine) allele in the first born twin was more common and considered protective for the development of RDS in newborn twins, and the C (threonine) allele can be considered as a susceptibility factor for acute respiratory distress syndrome. This conclusion coincides with our data.

The study of the 252A polymorphic locus of the LTA gene did not reveal significant differences in the genotype frequencies in patients with rdsH and in control 2 ($p = 0.24$). A rare genotype in the population was found in the subgroup of newborns with RDSH in 5.56%, in the subgroup "control 2" in 3.7% of cases. The homozygotes for the AA genotype prevailed in the "control 2" subgroup - 62.96%, whereas in the subgroup of patients with preterm, AO -51.85% heterozygotes prevailed against 33.33% in the "control 2" subgroup.

Significant differences are noted in the frequency distribution of Ivc alleles of the polymorphic locus 252A> in the LTA gene. In patients with RDSH, the allele frequency was 40.74% versus 20.37% in "control 2" ($p = 0.01$, $\chi^2 = 6.67$, OK. = 2.69.95% CI = 1.19-6.4) (Table 6). It can be assumed that the allele in is risky for the development of RDS in newborns. We did not find any data confirming or disproving our hypothesis, since studies of the LTA gene in newborns are few.

Thus, on the basis of risk factors, the most informative signs for the implementation of respiratory distress syndrome of newborns are determined. We believe that the simultaneous presence in the prognostic table of such signs as the need to carry out SDTD or mechanical ventilation from birth, and acute infections in the mother during pregnancy suggests that the rdsn is caused not only by a surfactant deficiency. This statement confirms that the syndrome includes two loci of interleukin genes: 3953 C> T of the I-1B gene proposed by O.SusuPlag1 (2007) by the candidate prenatal infection and preterm labor and EAR polymorphism of the 11-1KM gene, studied mainly connection with premature delivery [Veyakg N. el al., 2004]. Syndromic analysis of the data determined that patients with RDSH are characterized by very low body weight from 1015 to 1387, which confirms the leading role of body weight as a criterion of maturity and survival of the child. The Apgar score on the 5 minute 2-4 points indicates that the development of the RDSN is influenced by the resuscitation.

Maternal age, a factor affecting ovogenesis [Mandrykina Zh.A., 2008], demonstrated that for mothers who gave birth to an RDSH patient, the period up to 23 years and over 31 years is decisive. Thus, the prognosis of RDSN development is determined by a complex of factors, of which the most important are biological: HFPN and maternal infections during this pregnancy, fetal body

weight, birth asphyxia; and pathogenic (ongoing resuscitation).

At the fourth stage of the study, we carried out a comparative analysis of the influence of sociodemographic, ante - and intrapartum risk factors, clinical and anthropometric parameters, polymorphic genotypes and alleles between subgroups of patients with respiratory disorders complicated by sepsis and without it. For the vast majority of indicators, no differences have been identified. Statistically significantly only the distribution of alleles of the POTA polymorphism of the I, -1S gene was rare: the AZ allele rare in the population was found in newborns in the sepsis-group in 5.26% of cases and was completely absent in the sepsis + group ($p = 0.04$). However, since the confidence interval for the odds ratio contains zero, we cannot recognize this factor as protective. With a certain degree of probability, it is possible to state the possible influence of the 1b-1 III genotype on the addition of infectious complications to respiratory disorders.

Comparative analysis of clinical and laboratory parameters observed in newborns with respiratory disorders at the 1-2nd, 3-6th days of life and at the age of 7 or more days did not find a statistically significant difference in the studied subgroups. A significant difference is noted in the change in the number of neutrophils in newborns in the "sepsis +" subgroup, compared to the "sepsis-" subgroup on the 1-2 day of life. In patients with sepsis, a higher level of neutrophils is observed: $12.2 \cdot 10^9$ versus $10.3 \cdot 10^9$ in 1 ml of blood in the sepsis-subgroup ($p = 0.031$). However, it is worth noting that both indicators are not a criterion for leukocytosis for newborns on the 1st day of life, but are included in the age norm.

Prediction of sepsis, which complicated the respiratory disorders of the newborn, was made in the SAND program. It is established that the most informative sign for sepsis is the presence of multiple organ failure. In addition, the syndromic diagnosis included the signs that determine the quantitative composition of the blood corpuscles on different days of life and the level of glycemia. However, due to the low success rate of detections (less than 95), we cannot use the aforementioned symptoms for the decision rule of diagnostics, i.e. proper to predict the development of sepsis in newborns with respiratory disorders.

Conclusion

1. Risk factors for pneumonia in full-term newborns are: preeclampsia, chronic placental insufficiency, placental abruption, operative delivery from the mother, male gender, asphyxia at birth. Risk factors for respiratory distress syndrome in premature newborns are: chronic placental insufficiency, acute inflammatory diseases of the mother during this pregnancy.

2. Allele C of the polymorphic locus 15800T 4 of the BITV exon gene and the allele in the polymorphic locus 252A> 0 of the LTA gene are risk factors for the development of respiratory distress syndrome of the newborn.

3. Possible computational prediction of the risk of pneumonia and respiratory distress syndrome in newborns using prognostic tables.

4. Polymorphic variants of the I-1S gene are associated with the development of infectious complications (sepsis) in newborns.

LITERATURE:

1. Bogdanova R.Z., Fatykhova A.I., Danilko K.V., Viktorov V.V., Viktorova T.V. Genetic markers of respiratory disorders in newborns // Bulletin of the Ural Medical Academic Science. - 2008. - № 4. - p. 44-48.
2. Bogdanova R.Z., Fatykhova A.I., Danilko K.V., Viktorov V.V., Viktorova T.V. Genetic markers of respiratory disorders in newborns // Questions of practical pediatrics. - 2008. - Vol. 3, No. 6. - P. 12-16.
3. Bogdanova R.Z., Tsydenzhapov E.T., Fatykhova A.I., Viktorov V.V., Viktorova T.V., Mironov P.I. Genetic markers of predisposition to infectious diseases in newborns with respiratory distress syndrome // Anesthesiology and Resuscitation. - 2009. - № 1. - p. 46-48.
4. Danilko K.V., Khamidullina L.I., Fatykhova A.I., Fayzullina P.M., Bogdanova R.Z., Viktorova T.V. Gene angiotensin-converting enzyme (ACE) and susceptibility to the development of respiratory disorders of newborns // Medical genetics. - 2009. - № 9. - p. 38-43.
5. Danilko K.V., Bogdanova R.Z., Fatykhova A.I., Viktorov V.V., Viktorova T.V. Cytokine gene polymorphism (TNF-a, LTA, IL-1B, IL1-RN, IL-10) in newborns with respiratory distress syndrome // Scientific breakthrough 2004: collection of scientific papers of the conference of scientists of the Republic of Belarus. - Ufa, 2004. - p. 13 -14.
6. Fatykhova A.I., Viktorov V.V., Mironov P.I., Bogdanova R.Z., Shamsutdinova Ch.M. Using the criteria for systemic inflammatory response in the diagnosis and treatment of neonatal sepsis // Modern technologies in pediatrics and pediatric surgery: Proceedings of the Russian Congress. - M., 2004. - p. 205.
7. Fatykhova A.I., Bogdanova R.Z., Viktorov V.V., Viktorova T.V., Danilko K.V. The role of cytokine genes (TNFA, LTA, IL-1B, IL-10) in the development of respiratory distress syndrome of the newborn // Pediatric anesthesiology and intensive care: materials of the Russian Congress. - M., 2005. - p. 262 - 263.
8. Fatikhova A.I., Viktorov V.V., Mironov P.I., Bogdanova R.Z., Shamsutdinova Ch.M. Modern diagnosis of neonatal sepsis // Materials of the V Congress of the Russian Association of Perinatal Medicine Specialists. - M., 2005. - p. 206 - 207.
9. Danilko K.V., Bogdanova R.Z., Fatykhova A.I., Viktorova T.V., Viktorov V.V. The role of interleukin 8,10 gene polymorphism in the development of respiratory distress syndrome in newborns // Medical Immunology. - 2005. - Vol. 7, No. 2-3: Days of Immunology in St. Petersburg: materials of the IX All-Russian Scientific Forum with international participation. Acad. IN AND. Ioffe - p. 183-184.
10. Yu. Danilko K.V., Bogdanova R.Z., Fatykhova A.I., Viktorova T.V., Viktorov V.V. Search for candidate genes for respiratory disorders syndrome in newborns // Medical genetics. - 2005. - T. 4, No. 4: Proceedings of the V Congress of the Russian Society of Medical Geneticists. - p. 177.
11. P. Danilko K.V., Bogdanova R.Z., Fatykhova A.I., Viktorova T.V., Viktorov V.V. Polymorphism of the 4th intron of the protein B surfactant gene in newborns with respiratory disorders // Pulmonology. -2005. - № 1: spec. edition: Materials of the 15th National Congress on Respiratory Diseases. - p.18.
12. Danilko K.V., Bogdanova R.Z., Fatykhova A.I., Akhmadishina L.Z., Viktorova T.V., Viktorov V.V. Genetic variants of interleukins 6, 1 and interleukin 1 receptor antagonist: association with neonatal respiratory disorders // Medical Immunology. - 2006. - Vol. 8, No. 2-3: Days of Immunology in St. Petersburg: materials of the X All-Russian Scientific Forum with international participation. Acad. IN AND. Ioffe - p. 309.

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