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On the Issue of Clinical and Functional Characteristics of Long-Term Respiratory Outcomes in Children Who Suffered Respiratory Distress Syndrome in The Neonatal Period

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Abstract

Respiratory distress syndrome (RDS) experienced in the neonatal period is considered a key factor in the development of chronic respiratory pathology in childhood. Despite a significant reduction in mortality thanks to the introduction of surfactant therapy and modern respiratory support methods, the issue of long-term respiratory outcomes remains poorly understood, particularly in the context of functional lung disorders in school-age children.

Keywords: Bronchopulmonary dysplasia, respiratory function, neonatology, pediatrics, chronic lung diseases.

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1. Introduction

Respiratory distress syndrome of newborns is one of the leading causes of respiratory failure in the early neonatal period, mainly in premature infants, in whom the immaturity of the surfactant system leads to a decrease in lung compliance and severe gas exchange disorders.

According to modern studies, the incidence of RDS in newborns with a gestational age of less than 32 weeks reaches 60–80%, which determines the high medical and social significance of this pathology. The introduction of modern intensive care technologies, including exogenous surfactant, non-invasive ventilation and gentle respiratory support regimens, has significantly increased the survival rate of newborns with RDS.

However, the increase in survival rate is accompanied by an increase in the number of children with long-term dysfunction of the respiratory system caused by damage to immature alveolar structures, inflammatory processes and impaired alveologenesis. The key pathogenetic mechanism for the formation of long-term respiratory disorders is the remodeling of lung tissue, including simplification of the alveolar structure, a decrease in the area of gas exchange and the development of bronchial hyperreactivity.

These changes are clinically manifested by a decrease in indicators of external respiratory function, in particular FEV1, as well as an increased frequency of broncho-obstructive syndromes and infectious diseases of the respiratory tract. A special place among complications is occupied by bronchopulmonary dysplasia, which develops

in a significant proportion of children who have suffered severe RDS and is characterized by chronic inflammation, fibrosis and impaired vascular development of the lungs. Such patients subsequently experience a persistent decrease in ventilation parameters, a decrease in SpO_2 during exercise, and a high frequency of hospitalizations for respiratory pathology.

Despite the presence of a significant number of studies devoted to the neonatal period, the problem of long-term functional outcomes in older children remains insufficiently studied, especially in the context of a comprehensive assessment of clinical and functional parameters. The lack of systematic data makes it difficult to develop effective strategies for monitoring and preventing chronic respiratory diseases.

The problem is given additional relevance by the increasing frequency of broncho-obstructive conditions in children who have suffered from RDS, which requires clarification of the mechanisms of their formation and identification of risk factors. In modern conditions, the use of objective methods for assessing the function of external respiration, such as spirometry, which makes it possible to identify hidden disorders of the ventilation function, is of particular importance.

From the perspective of evidence-based medicine, it is important to conduct comprehensive clinical and functional studies including objective indicators, such as FEV1, SpO_2, the frequency of obstructive episodes and infectious complications, which will allow a more accurate assessment of the state of the respiratory system in this category of patients. The scientific gap lies in the insufficient knowledge of the relationship between the severity of RDS in the neonatal period and the severity of functional disorders of the respiratory system in later life, as well as the lack of unified approaches to long-term monitoring of such patients.

The purpose of this study is a comprehensive assessment of the clinical and functional characteristics of long-term respiratory outcomes in children who suffered respiratory distress syndrome in the neonatal period. To achieve this goal, the following tasks were identified: analysis of indicators of pulmonary function (FEV1), assessment of the level of oxygen saturation (SpO_2), study of the frequency of bronchial hyperreactivity and obstructive episodes, as well as identifying the frequency of infectious complications and risk factors for their development.

The results obtained are important for improving the dispensary observation system, developing preventive measures and increasing the effectiveness of treatment for children with RDS, which ultimately helps to improve the quality of life of patients and reduce the burden of chronic diseases of the respiratory system.

The design of the study was prospective-retrospective cohort in nature and was aimed at a comprehensive assessment of the clinical and functional state of the respiratory system in children who suffered respiratory distress syndrome (RDS) in the neonatal period. The study was conducted in specialized pediatric institutions in compliance with the principles of evidence-based medicine and ethical standards (informed parental consent, anonymization of data). The main group included 124 children aged 6 to 10 years with a documented history of RDS.

Inclusion criteria were: gestational age less than 34 weeks, the presence of clinically confirmed RDS in the neonatal period, and the absence of congenital malformations of the respiratory system. The control group consisted of 62 practically healthy children of comparable age without a history of severe neonatal pathology. Data collection included analysis of medical documentation (neonatal history, duration of mechanical ventilation, use of surfactant therapy), as well as clinical examination at the time of inclusion in the study.

Particular attention was paid to the frequency of episodes of bronchial obstruction, the number of acute respiratory infections experienced over the past year and the presence of hospitalizations. Functional assessment of the respiratory system was performed using standardized spirometry methods. Forced expiratory volume in the first second (FEV1), forced vital capacity (FVC), and FEV1/FVC ratio were measured. The indicators were interpreted as a percentage of the proper values, taking into account the age, height and gender of the child.

Additionally, pulse oximetry (SpO_2) was performed at rest and after standardized physical activity (six-minute walking test), which made it possible to assess the reserve capabilities of the respiratory system and identify hidden gas exchange disorders. Bronchial hyperresponsiveness was assessed based on clinical data (presence of wheezing episodes, response to bronchodilators). Statistical data processing was carried out using parametric and nonparametric analysis methods.

To assess the significance of differences, the Student test and χ^2 test were used. Differences were considered

statistically significant at $p < 0.05$. Results are presented as means (M ± SD) and percentages.

Analysis of the obtained data revealed significant differences between the main and control groups in key clinical and functional indicators of the respiratory system. In children who suffered from RDS, there was a persistent decrease in respiratory function indicators, as well as a higher incidence of respiratory complications. The FEV1 indicator in the main group averaged 78.4 ± 6.2% of the expected values, while in the control group this indicator reached 96.1 ± 4.8% ($p < 0.001$), which indicates the presence of obstructive ventilation disorders in the examined patients.

A decrease in the FEV1/FVC ratio also indicated the formation of chronic obstructive airway dysfunction. The level of oxygen saturation (SpO_2) at rest in most cases was within the normal range, however, during a stress test, 27.4% of children in the main group showed a decrease in SpO_2 below 95%, which indicates a violation of ventilation-perfusion processes and limited adaptive capabilities of the respiratory system.

The frequency of bronchial hyperreactivity in children who suffered from RDS was 38.7%, which significantly exceeds the same figure in the control group (12.9%, $p < 0.01$). Clinically, this manifested as episodes of wheezing, coughing, and the need to use bronchodilators. Particular attention is drawn to the high frequency of infectious complications: the average number of acute respiratory infections in the main group was 5.2 ± 1.4 episodes per year, while in the control group it was 2.3 ± 0.9 ($p < 0.001$). At the same time, 18.5% of children in the main group had repeated hospitalizations associated with broncho-obstructive conditions.

Additional analysis showed that the severity of functional impairment correlates with the severity of RDS in the neonatal period and the duration of mechanical ventilation. In children who were on mechanical ventilation for more than 7 days, the decrease in FEV1 was more pronounced (up to 70–75% of normal), and the frequency of bronchial hyperreactivity reached 45%.

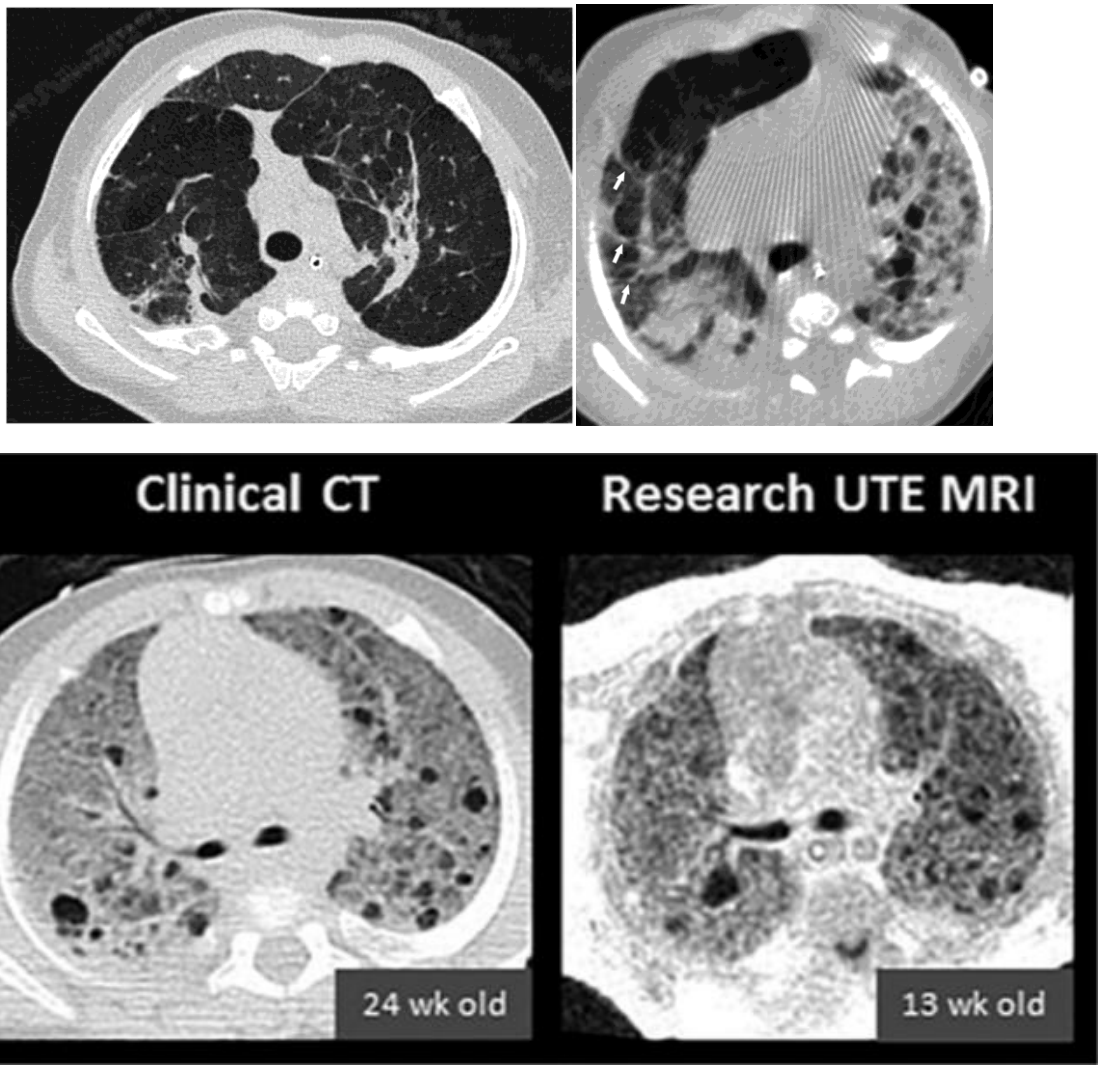
The results obtained convincingly demonstrate that RDS suffered in the neonatal period has a long-term negative effect on the functional state of the respiratory system, forming persistent ventilation disorders, a decrease in the reserve capacity of the lungs and an increased susceptibility to infectious agents.

The data obtained during the study confirm that respiratory distress syndrome (RDS) suffered in the neonatal period has a stable and clinically significant effect on the formation of the functional state of the respiratory system in subsequent years of life. The revealed decrease in FEV1 indicators, an increase in the frequency of bronchial hyperreactivity and infectious complications are consistent with the results of international cohort studies, which also show that children who have suffered from RDS develop signs of chronic obstructive pathology of the respiratory tract already in preschool and school age.

A comparative analysis with foreign studies demonstrates a similar trend: the decrease in FEV1 in children with a history of RDS varies within 10–25% of the expected values, while the severity of the disorders directly correlates with the severity of the neonatal period and the duration of respiratory support. Our data (15–23% reduction in FEV1) are in a comparable range, which confirms their reliability and reproducibility. The key pathogenetic mechanism for the formation of the identified disorders is damage to the alveolar apparatus during the critical period of postnatal lung development.

Immature lung tissue in premature newborns is characterized by high vulnerability to mechanical and oxygen influences, which leads to disruption of alveologenesis processes and the formation of a simplified structure of the alveoli. This, in turn, causes a decrease in the gas exchange area and the formation of persistent ventilation disturbances.

Rice. 1. CT signs of bronchopulmonary dysplasia



An equally significant factor is hypoxia, which accompanies the course of RDS and has a systemic effect

on the developing lung tissue. Chronic or intermittent hypoxia leads to impaired angiogenesis and remodeling of the pulmonary vascular bed, which worsens ventilation-perfusion relationships. In our study, this is confirmed by a decrease in SpO_2 during physical activity in a significant proportion of children, which indicates insufficient compensatory ability of the respiratory system. The inflammatory component also plays a key role in the pathogenesis of long-term respiratory disorders.

Persistent inflammation initiated in the neonatal period promotes airway remodeling, thickening of the bronchial wall and increased receptor sensitivity, which is clinically manifested as bronchial hyperresponsiveness. The high frequency of broncho-obstructive episodes we identified confirms the significance of this mechanism.

From the standpoint of clinical practice, the identified increased frequency of infectious complications in children who have suffered from RDS is of particular significance. This phenomenon may be due to impaired mucociliary clearance, decreased local immunity and structural changes in the respiratory tract. An increase in the frequency of acute respiratory infections by 1.8–2.3 times compared to the control group confirms the presence of persistent functional vulnerability of the respiratory system. Analysis of risk factors showed that the degree of prematurity, duration of mechanical ventilation and severity of RDS have the greatest influence on the formation of adverse outcomes.

Long-term mechanical ventilation is associated with baro- and volutrauma, which increases damage to lung tissue and contributes to the development of bronchopulmonary dysplasia. In children who were on mechanical ventilation for more than 7 days, there was a more pronounced decrease in FEV1 and a high frequency of bronchial hyperreactivity, which indicates a dose-dependent effect of damaging factors.

The long-term consequences of RDS go beyond purely functional impairment and include the formation of prerequisites for the development of chronic lung diseases, including early manifestations of chronic obstructive pulmonary disease. Considering that the peak development of lung tissue occurs in the first years of life, any disorders during this period are prolonged in nature and can determine the state of the respiratory system in adulthood. Taking into account the data obtained, the need for early risk stratification and the formation of individualized monitoring programs for children who have suffered RDS becomes obvious.

Of particular importance is regular monitoring of respiratory function indicators (FEV1), assessment of oxygen saturation (SpO_2), as well as timely diagnosis of bronchial hyperreactivity. The results of the study confirm the multifactorial nature of the formation of long-term respiratory outcomes, which is based on a combination of structural, functional and inflammatory changes in lung tissue. The identified patterns are of fundamental importance for the development of preventive and treatment strategies aimed at reducing the burden of chronic respiratory pathology in children who have suffered RDS in the neonatal period.

The study made it possible to establish that respiratory distress syndrome suffered in the neonatal period has a prolonged and clinically significant effect on the functional state of the respiratory system in children. The results obtained demonstrate the formation of persistent ventilation disorders, manifested by a decrease in FEV1 values, disturbances in ventilation-perfusion ratios and an increased frequency of bronchial hyperreactivity.

Analysis of clinical and functional indicators showed that in children with a history of RDS, there is a statistically significant decrease in the function of external respiration, as well as a tendency to decrease the level of SpO_2 during physical activity, which indicates an insufficiency of the reserve capacity of the pulmonary system. The revealed increase in the frequency of broncho-obstructive episodes and infectious complications confirms the presence of chronic functional vulnerability of the respiratory tract.

From the point of view of pathogenesis, it has been established that damage to the alveolar apparatus, hypoxic exposure and persistent inflammation in the neonatal period play a key role in the formation of long-term disorders. These factors lead to remodeling of the lung tissue, a decrease in the area of gas exchange and an increase in the sensitivity of the airways, which is subsequently manifested by clinical symptoms of obstruction and a decrease in ventilation rates. The identified relationship between the severity of RDS, the duration of artificial ventilation and the severity of functional impairment indicates the need for early stratification of patients according to risk level.

Children who have suffered severe forms of RDS require closer and longer follow-up with regular assessment of respiratory function and clinical status. The practical significance of the study lies in substantiating the need to implement programs for early monitoring and prevention of chronic diseases of the respiratory system in this category of patients.

Early diagnosis of pulmonary function disorders, timely correction of bronchial hyperreactivity and prevention of infectious complications can significantly reduce the risk of developing chronic pathology and improve the quality of life of children. Prospects for further research are related to an in-depth study of the molecular cellular mechanisms of damage to lung tissue, as well as the development of personalized approaches to the rehabilitation and treatment of children who have suffered respiratory distress syndrome. Particular attention should be paid to the integration of modern methods of functional diagnostics and biomarkers of inflammation into clinical practice.

Respiratory distress syndrome of newborns should be considered not only as an acute condition of the neonatal period, but also as a significant risk factor for the development of chronic respiratory disorders that require comprehensive and long-term medical support.

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