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Genetic Characteristics of the Hemostasis System in Early Children with Pneumonia

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Summary: The article presents information about the study of the features of the course of pneumonia in children, changes in the hemostasis system, features of genetic polymorphism in various inflammatory diseases. An acute inflammatory process in the lungs leads to a violation of their metabolic function, disrupts the balance of the hemostasis system of the lungs. According to the results of laboratory and instrumental examination in children with pneumonia, significant changes in the hemostasis system were revealed

Keywords: children, pneumonia, hemostasis, genetic polymorphism

Actuality

Outpatient pneumonia (VP) po-prejnemu yavlyaetsya vedushchey prichinoy smerti sredi detey v vozraste do 5 let vo vsem mire: po otsenkam, v 2015 g. Umerlo 0.921 million people. In fact, VP is more advanced than the previous age group, which causes premature death in children with a high mortality rate in children under 5 years of age, but it is not necessary to have a middle and middle-aged child mortality rate. A feature of pneumonia in children is the frequent development of infectious-toxic shock with impaired hemostasis [3,7,10] according to the type of consumption phase - DIC [6,7,12,16]. An acute inflammatory process in the lungs leads to a violation of their metabolic function, which manifests itself in the loss of the ability of the lungs to regulate the balance of proteases-antiproteases of the hemostasis system [3].

Pneumonia is one of the most common respiratory diseases in children of different age groups. Currently, there are single studies devoted to the study of the state of the hemostasis system in pneumonia in children. Despite advances in diagnostic methods and antibiotic therapy, community-acquired pneumonia (CAP) remains the leading cause of morbidity and mortality worldwide.

The risk of CAP is associated with pathogen virulence, host susceptibility, and epidemiological factors. A significant number of CAP patients develop severe complications such as sepsis, acute respiratory distress syndrome (ARDS), multiple organ dysfunction syndrome (MODS) and less fatal conditions (pleurisy, empyema) and syndromes (acute respiratory failure (ARD)). The variety of clinical manifestations of CAP suggests a genetic predisposition [1]. The susceptibility to CAP and critical complications of CAP has been systematically studied by several groups of researchers and the important role of some host genetic variations in the variety of clinical manifestations of CAP has been established [1,3,9] Host response systems such as pattern recognition pathway, inflammatory molecules, antioxidant defense and coagulation mechanism blood likely play a role in this variable response to VP. Common diseases are known to have complex etiologies, such as dependence of genotypic effects on environmental factors (gene-environment interactions) and genotypes at other loci (gene-gene interactions). The success of pathway-based analysis in research on various diseases suggests that pathway-based methods are of great value in linking different disease phenotypes. A strategy that goes beyond single gene analysis usually provides insight into the underlying molecular mechanisms.

An acute inflammatory process in the lungs leads to a violation of their metabolic function, which manifests itself in the loss of the ability of the lungs to regulate the balance of proteases-antiproteases of the hemostasis system [3]. The state of this problem in pediatrics dictates the need for more extensive research and substantiated conclusions about the state of the hemostasis system. The polygenic approach as a tool for identifying individuals at increased risk of complications suggests that the simultaneous presence of several genetic variations with weak but significant effects on the hemostasis process may affect the risk of serious thrombotic complications. Polymorphisms of the genes of the hemostatic system Fibrinogen (factor I) is one

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of the main factors of the coagulation system, which is involved in the process of hemostasis. In addition to its role in the coagulation reaction, fibrinogen is involved in the pathogenesis of atherosclerosis by promoting platelet and leukocyte adhesion to the endothelial surface and modulating plasmin binding to its receptor. Fibrinogen circulates in plasma as a dimer. The mature fibrinogen protein consists of two chains, each of which in turn consists of alpha, beta and gamma polypeptides, which are encoded by the FGA, FGB and FGG genes located in the same cluster on chromosome 4. SNPs associated with differences in plasma fibrinogen levels.

Minor alleles of four polymorphisms in the FGB gene, two in the FGA gene, and one polymorphism in the FGG gene are associated with elevated plasma fibrinogen levels. SNPs in the FGB gene promoter (–455GA, rs1800790) and in the FGA gene promoter (58GA, rs2070011) affect plasma fibrinogen levels.

The large multimeric glycoprotein von Willebrand factor (VWF), secreted by vascular endothelial cells, has a five-fold variability in the level of antigen in the blood plasma of healthy people, functions as an antihemophilic factor and interface between the platelet and the vascular wall in the blood coagulation system. VWF plays a key role in the process of hemostasis and the formation of arterial thrombosis, acting as a molecular bridge that binds platelets to damaged endothelium, and as a carrier molecule for coagulation factor VIII, facilitating platelet adhesion to normal endothelium and platelet aggregation at sites of vascular injury [12,13]. Low levels of VWF are associated with bleeding, while elevated levels are associated with the risk of thrombosis, MI, and stroke. Plasma levels of VWF are 53–75% dependent on genetic factors and contribute to the genetic predisposition to CVD [14]. Elevated plasma levels of VWF are an independent risk factor for venous thromboembolic disease, MI, and stroke [18,19]. The role of VWF in arterial thrombosis and atherosclerosis makes it a useful clinical marker of atherosclerotic risk. VWF is associated with endothelial dysfunction and the pathogenesis of atherosclerosis due to its ability to mediate platelet adhesion. An association between SNP rs216809 in the VWF gene (von Willebrand factor) and carotid plaque thickness was revealed [5].

The thrombotic phenotype is associated exclusively with genes that control coagulation and hemostasis, especially with the F5 and P2RY12 genes. [14,15]. Testing of an additive model from a number of common prothrombotic polymorphisms (F2 20210GA, SERPIN1 4G/5G, FGB -455GA, FV Leiden, F7 -402GA and -3ID, P2Y12 -744TC, Platelet Glycoprotein Ia 873GA and Platelet Glycoprotein IIIa 1565TC).
Plasminogen activator inhibitor (PAI)-1 inhibits urokinase and tissue plasminogen activator required for host response to infection. It is not known whether changes in the PAI-1 gene are associated with increased susceptibility to infection. The role of 4G/5G polymorphism and other genetic variants in the PAI-1 gene that variants associated with increased expression of PAI-1 will be associated with an increase in community-acquired pneumonia (CAP). [1,2]
Conclusion. The complex interaction between genetic and environmental factors in the pathogenesis of complex diseases with a proven genetic component, such as bronchopulmonary pathology, pneumonia and biofeedback, in which the influence of individual genes on risk is weak, explains why functional polymorphism can affect not only the intermediate (platelet activation), but also on the clinical phenotype (eg, alveolitis).
This observation is consistent with the concept that in multifactorial diseases, genetic polymorphisms more often affect the risk of the disease, determining individual sensitivity to environmental risk factors, rather than being the cause of the pathological process itself [20]. Many authors believe that genotyping for individual polymorphisms is useless for clinical assessment of the individual risk of bronchopulmonary pathology and its complications, and that it is necessary to genotype patients using a panel of hemostasis and coagulation markers [3, 4, 15, 16, 17,19]. In particular, the combination of prothrombotic polymorphisms can help predict community-acquired pneumonia in children [4].

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