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Yarmukhamedova N. ✉, Khadjimetov A., Rizaev J.
Samarkand State Medical Institute, Samarkand, Uzbekistan

Features of Chronic Viral Infections with Combined Gastrointestinal Tract Damage in Adolescent Athletes

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Contacts: nargiza_ya@inbox.ru

Abstract

Some aspects of combined damage to the respiratory and gastrointestinal tracts in chronic viral infections in adolescent athletes have been studied. 125 young athletes aged 11–17 years were examined. The PCR method was used to detect the virus, the enzyme immunoassay method for the determination of defensin, neopterin and cathelicidin in blood serum. It was revealed that in adolescent athletes, rotavirus is the predominant pathogen in the oral mucosa and gastrointestinal tract, and the most common combined lesion develops with enterovirus infection, as well as an increase in antimicrobial peptides in the blood serum.
Keywords: chronic viral infections, gastrointestinal tract damage, adolescent athletes

Ярмухамедова Н.А. ✉, Хаджиметов А.А., Ризаев Ж.А.
Самаркандский государственный медицинский институт, Самарканд, Узбекистан

Особенности хронических вирусных инфекций с сочетанным поражением желудочно-кишечного тракта у спортсменов-подростков

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Контакты: nargiza_ya@inbox.ru

Резюме

Изучены некоторые аспекты сочетанного поражения дыхательных путей и желудочно-кишечного тракта при хронических вирусных инфекциях у спортсменов-подростков. Обследовано 125 юных спортсменов в возрасте 11–17 лет. Для обнаружения вируса использовали метод ПЦР, метод иммуноферментного анализа для определения дифенсина, неоптерина и кателицидина в сыворотке крови. Выявлено, что у спортсменов-подростков ротавирус является преобладающим возбудителем слизистой оболочки полости рта и желудочно-кишечного тракта, а наиболее частым сочетанным поражением является энтеровирусная инфекция, а также повышение антимикробных пептидов в сыворотке крови.

Ключевые слова: хронические вирусные инфекции, поражение желудочно-кишечного тракта, спортсмены-подростки

■ INTRODUCTION

According to literature sources, children suffering from repeated viral infections of the respiratory tract make up from 20% to 65% of the child population. Up to 80% of all cases of acute upper respiratory tract infections (URTs) in children, they are caused by viral agents, bacteria are in second place with a significant lag. Recurrent respiratory infections can be caused by Streptococcus pneumoniae, Streptococcus pyogenes, Staphylococcus aureus, Moraxella (Branhamella) catarrhalis, Haemophylus influenzae bacteria (most commonly type b); viruses (mainly respiratory syncytial virus, influenza viruses, parainfluenza, adenoviruses); pathogens of the Chlamydia and Mycoplasma family and other agents. It should be noted that the leading ARI syndromes are catarrhal and hyperthermic, at the same time, symptoms of gastrointestinal tract (gastrointestinal tract) damage in the form of abdominal pain, dyspepsia and diarrhea often join the traditional clinical picture. This may be due to several reasons: the characteristics of the pathogen, combined infection with agents that are tropic to the respiratory system and gastrointestinal tract, as well as the side effect of drugs used in therapy.

Currently, about 200 viruses are known to be the causative agents of ARI and AII. Almost every year, new viruses with special properties are discovered. In addition to the pathogens of ARI and AII with selective damage to one system, viruses that cause combined lesions of both the respiratory and gastrointestinal tracts have recently attracted attention. In particular, with coronavirus infection, along with respiratory symptoms, 7.5% have vomiting, 10% have diarrhea. The problem of mixed infection is extremely relevant today, according to some data, up to 30% of AII have a combined etiology.

It was found that with an increase in the number of acute respiratory viral infections, the frequency and spectrum of germinated microorganisms increases. It should be noted that the frequency of infections is affected by a whole complex of factors; an annual outbreak of influenza and flu-like diseases, which reduces immunological resistance and leads to secondary bacterial complications, mucociliary and surfactant system, features of the structure of the bronchi, delayed development of the immune system, social living conditions, as well as the composition of the microflora of the respiratory tract and gastrointestinal tract. At the same time, the mucous membrane of the upper respiratory tract and gastrointestinal tract, having lost its own immune protection, becomes vulnerable to bacterial pathogens that receive conditions for their reproduction and persistence, respiratory and intestinal dysbiosis is formed. In addition, pronounced violations of microbiocenosis, which reduce resistance to pathogenic pathogens and contribute to the violation of the integrity of the epithelial barrier, support a long-term inflammatory process and the development of chronic intoxication. In our opinion, dysbiotic changes in the respiratory and gastrointestinal tract of the tract cannot but have their negative impact on the functional properties of the respiratory and digestive organs, including the state of the water-salt balance, phospholipid composition of the mucosa, etc. With combined infection with intestinal

and respiratory viruses, there is a more severe course of the infectious process, mixed symptoms, and a high frequency of post-infectious viral and bacterial transmission. In the works of corresponding member of the Russian Academy of Sciences A.V. Gorelov, Doctor of Medical Sciences A.A. Ploskireva, Doctor of Medical Sciences N.H. Thakushinova, the spectrum of manifestations of rotavirus infection, including both gastrointestinal and respiratory symptoms, was studied, and the predominance of the latter during repeated infection was shown. So, the problem of acute infections of the respiratory and gastrointestinal tract of the tract is relevant and has a number of aspects. It should be noted that until recently, neither epidemiologists nor clinicians paid due attention to the problem of combined damage to various body systems in a number of infections. Given the lack of data in the literature on the impact of chronic viral infections with combined gastrointestinal tract damage in adolescent athletes, we believe that the study of these relationships in adolescents with recurrent respiratory diseases is of not only scientific but also practical interest. The purpose of this study was to evaluate some aspects of combined damage to the respiratory and gastrointestinal tracts in chronic viral infections in adolescent athletes.

■ MATERIALS AND METHODS

In order to identify biomedical and socio-hygienic factors affecting the health of children and adolescents involved in youth sports schools, 125 young athletes aged 11–17 years of Samarkand were surveyed and interviewed. This age is chosen because 11 years is the age at which sports specialization begins in many sports. The sample included children and teenagers who have been involved in sports for more than one year, performing at competitions, representing such sports as football, basketball, volleyball, tennis, table tennis, athletics. The material collection program provided for copying information from primary medical documentation. All data were entered into a specially developed "Map of the study of the morbidity of children and adolescents of children's and youth sports schools according to the data of the appeal". Diagnoses of ARI, AII and their etiology were established on the basis of the clinical picture and laboratory (according to a complex of bacteriological, virological and immunological methods). To identify and determine the type of respiratory viruses in nasopharyngeal smears, the multiplex PCR method was used with hybridization-fluorescence detection of amplification products with a set of reagents "AmpliSens ARVI-screen-FL" (FBIS Central Research Institute of Epidemiology of Rospotrebnadzor, Russia). Polymerase chain reaction with real-time fluorescence detection (PCR-RV) for the presence of appropriate nucleic acids with a set of reagents "AmpliSens AII-screen" (FBIS of the Central Research Institute of Epidemiology of Rospotrebnadzor, Russia) was used to detect a wide range of pathogens of viral AII (adeno-, entero-, noro-, astro-, reoviruses). In order to identify bacterial pathogens of AII, a bacteriological examination of the feces of all patients was carried out. Using the enzyme immunoassay, the quantitative content of defensin, neopterin and cathelicidin in the blood serum was determined by the kits of Biochemmak (Russia). Mathematical and statistical methods were used to process the data obtained at each stage of the study. Relative values, representativeness errors, and the reliability of differences in indicators according to the Student's criterion were calculated (the differences were considered reliable at $p<0.05$).

■ RESULTS AND DISCUSSION

Currently, there is a hypothesis that SARS affect the composition of the microbiota of the upper respiratory tract, and the microbiota, in turn, also affects the susceptibility to SARS and their severity. Thus, it was shown that microbiota variants in children of the first year of life with a predominance of Corynebacterium, Alloiococcus (Dolosigranulum) and Staphylococcus are associated with a lower risk of developing acute respiratory viral infections, and microbiota variants with a predominance of Moraxella, Streptococcus and Haemophilus are at increased risk. However, the data on the study of microbiota and its relationship with ARVI are somewhat contradictory, which requires additional study.

In the course of the study in adolescent athletes, we identified the etiology of infectious lesions of the respiratory and gastrointestinal tract, in 78.4% of adolescent athletes. It should be noted that rhinovirus prevails in the structure of pathogens of chronic respiratory infection in adolescents, rotavirus and enterovirus predominate in the structure of acute intestinal infection, mixed infections were registered in 31.5% of children of this group. The revealed results allow us to consider this problem not only from the standpoint of polysystemic manifestations of individual infections, but also infectious polymorbidity. In-depth analysis of the etiological structure of pathogens of chronic respiratory infection, as well as intestinal infection showed that adenovirus is detected on average in 6.7% of athletes, rotavirus – in 79.6% of athletes, enterovirus – in 12.6% of adolescent athletes. It should be noted that the combined infections that often occur in the examined adolescents, which are combined with various chronic pathologies, which can cause exacerbation of chronic disease. At the same time, the severity of the gastrointestinal tract lesion was assessed by the presence and severity of exicosis, intoxication, temperature, prevalence of the lesion, duration of the main symptoms of the disease in days.

Analysis of the results showed that rotavirus is the most frequent causative agent of infections of the oral mucosa and gastrointestinal tract. At the same time, moderate symptoms are usually observed from the upper parts in the form of nasal congestion and runny nose, cough and pharyngeal hyperemia. The observed adenovirus infection was characterized by the predominance of gastrointestinal symptoms. It should be noted that one of the most frequent symptoms of adenovirus was flatulence.

In adolescent athletes, respiratory tract damage in case of infection of the oral mucosa and gastrointestinal tract occurred in the form of pharyngitis, rhinitis, rhinosinusitis and affected the severity of the course and the overall duration of the disease. A distinctive feature of the course of adenovirus infection in some adolescents was the development of conjunctivitis. From the data given, it follows that influenza, adenovirus infection and rotavirus infection are the most severe.

The most common complication of digestive tract infections is exicosis, which has occurred in almost a third of adolescents. At the same time, in 2.6% of cases in children against the background of gastrointestinal infection, a picture of an acute abdomen developed due to intussusception, acute mesadenitis, pancreatitis. It should be noted that 6.7% of adolescent athletes have a burdened allergic background. In the presence of this contingent of examined adolescents with gastroenterological pathology, anemia of chronic diseases was observed. Thus, the study of the microbiocenosis of the upper floor of the respiratory tract and its relationship with the functional activity of the respiratory organs in adolescent athletes exposed to frequent respiratory infectious diseases is of undoubted scientific and practical interest.

With regard to the purpose of our study, it is practically important to study respiratory tract dysbiosis against the background of viral intoxication, which do not reduce resistance to pathogenic pathogens and contribute to the violation of the integrity of the epithelial barrier, but also support the long-term inflammatory process and the development of chronic intoxication. In our opinion, dysbiotic changes in the respiratory tract cannot but have a negative impact on the functional properties of the respiratory organs, including the state of the endobronchial electrolyte balance, phospholipid composition of the superficially active lining of the lungs, and bronchial sensitivity.

The normal microflora of the oral mucosa is represented by a special ecological variety of streptococci and others colonize buccal epithelial cells, providing colonization resistance of the organism, that is, resistance to colonization by random, including pathogenic microorganisms for this ecological niche. Adolescents who had ARVI had the lowest rates of natural colonization of the buccal epithelium of normal flora. Moreover, they had colonization of the mucous membranes of the oral cavity with pathogenic flora, especially often Staphylococcus aureus. In turn, the bacterial carrier of Staphylococcus aureus affects the resistance of the host organism, which can lead to the development of diseases of a different etiology. Staphylococci have the ability to degrade immunoglobulins of various classes, deplete the complement system, lead to impaired functioning and cooperation of the immune response, the development of delayed hypersensitivity, disrupt the processes of phagocytosis, inhibit the activity of nonspecific resistance factors (lysozyme, DNase, RNase, muramidase and peroxidase), disrupt the processes of phagocytosis. This leads to a further decrease in the resistance of the organism and prolongation of the persistence of the pathogen.

The long-term existence of staphylococci in the body, distracting part of the reserves of specific and nonspecific resistance, is manifested by frequent and prolonged diseases, including respiratory organs, which is most pronounced in adolescence. In conditions when an organism or a microorganism is exposed to powerful factors (antibiotic therapy, prolonged psychoemotional stress, physical exertion, etc.), the macroorganism-microbiota subsystems can be disrupted, the connections connecting them are destroyed, and they can even enter a state of aggression.

As is known, the normal microbiota of the respiratory tract mucosa, which includes not only bacteria, but also viruses, fungi, archaea, plays an important role in maintaining homeostasis and protecting against infections. It helps to suppress the growth and reproduction of potentially pathogenic microorganisms. The microbiota also stimulates the synthesis of antimicrobial peptides and class A immunoglobulins, which is necessary for the realization of innate immunity.

The protective factors of the mucous membrane can be divided into mechanical, chemical and biological. The first should include the epithelial barrier itself, represented by ciliated epithelial cells connected by dense intercellular contacts. Mucociliary clearance and turbulent air flow during coughing and sneezing also play an important role in the mechanical cleansing of the mucous membrane of the respiratory tract. Chemical factors include lacrimal fluid enzymes (lysozyme) and antimicrobial peptides contained in mucus – a- and p-defensins, cathelicidin, lactoferrin, as well as secretory immunoglobulin A. In addition, lymphoid tissue associated with the mucous membrane – MALT (mucosa associated lymphoid tissue) actively participates in the protection of the mucous membrane of the respiratory tract. Immune cells are localized in the own plate of the

mucous membrane (lamina propria): dendritic cells, macrophages, T- and B-lymphocytes, eosinophils, mast cells, neutrophils.

The epithelium actively participates in immune reactions by actively transporting immunoglobulins to the lumen of the respiratory tract, as well as by interacting with immune cells. The respiratory epithelium synthesizes cytokines interacting with dendritic (anti-gene-presenting) cells, macrophages, eosinophils, neutrophils and T-lymphocytes.

Defensins are peptides with a wide spectrum of antimicrobial activity (antiviral, antibacterial, antifungal, antiprotozoal). Being the most common antimicrobial peptides in humans, defensins play an important role in providing innate immunity. p-Defensins also ensure the maintenance of a dynamic balance of the microbiota of the mucous membranes. Cathelicidin is synthesized by neutrophils, macrophages, epithelial cells in response to infection and not only has antimicrobial activity, but also induces cell apoptosis.

Neopterin is a protein synthesized by mononuclears and macrophages in response to their stimulation by gamma interferon. Gamma interferon is the so-called immune interferon type 2, the production of which is activated during cytotoxic effects – viral infections, mitogens, autoimmune reactions, etc. Bacterial infections, in which the immune response is realized through other mechanisms – antibody synthesis and acute phase reactions, are usually accompanied by an increase in the production of leukocyte alpha interferon (type 1) are not associated with an increase in serum concentrations of neopterin. The study of this peptide in the blood serum of adolescent athletes with chronic viral infection showed an increase in neopterin by an average of 3.6 times relative to the indicators of the comparison group. This is probably due to a hyperergic immune response and indicates a high activity of autoimmune processes triggered by virus antigens. Defensins are known to be cationic peptides whose biological role is to form ion channels in the membranes of pathogenic bacterial cells.

The system consists of alpha-defensins (99% of serum defensins) contained only in neutrophils (primary or azurophil granules) and involved in the destruction of a phagocytosed bacterial cell and released into the blood during neutrophil activation; beta-defensins found in the epithelium of the respiratory tract and intestines; and theta-defensins (encoded by the "silent gene"). Beta-defensins are 3 proteins, two of which are inducible and reflect the innate immunity of the mucous membranes. In this study, we found a significant increase in the serum concentration of defensins by an average of 5.3 times in athletes of adolescent age relative to the indicators of the comparison group. This picture reflects the intensity of the functioning of phagocytosis as a non-specific cellular immunity.

At the same time, the contribution of the autoimmune mechanism of increasing the concentration of defensins due to local autoimmune reactions is not excluded.

Cathelicidin is a cationic protein found in peroxidase-negative granules of neutrophils (secondary, specific), lymphocytes, monocytes, epithelial cells of the gastrointestinal tract

Concentration of endogenous antimicrobial peptides in the blood serum of adolescent athletes

Examined groups	Neopterin, nmol/l	Defensins, ngr/ml	Cathelicidin, ngr/ml
Comparison group	5.73±0.15	35.90±0.54	1.58±0.03
Main group	45.32±1.76*	187.36±3.91*	4.05±0,.13*

Note: * differences relative to data of 1st group are significant P<0.05.

and lungs. It has a synergistic antibacterial effect with defensins against gram-positive, gram-negative bacteria, protozoa and fungi. In addition, its C-terminal fragment is able to bind to lipopolysaccharides of the bacterial wall, preventing the development of infectious-toxic shock and causing chemoattraction of neutrophils and monocytes to the focus of infection. In this study, as expected, we found a significant ($p<0.05$) increase in the concentration of cathelicidin in adolescent athletes [1–41].

■ CONCLUSIONS

1. Rhinovirus prevails in the structure of pathogens of chronic respiratory viral infection in adolescents, rotavirus and enterovirus predominate in the structure of acute intestinal infection, mixed infections were registered in 31.5% of children of this group, which allows us to consider this problem not only from the standpoint of polysystemic manifestations of individual infections, but also infectious polymorbidity.
2. In adolescent athletes, the predominant pathogen in the oral mucosa and gastrointestinal tract is rotavirus, and the most common combined lesion develops with enterovirus infection.
3. The most frequent complication of infections of the digestive tract is exicosis, which occurred in almost a third of adolescents. At the same time, in 2.6% of cases, a picture of an acute abdomen developed in children against the background of a gastrointestinal infection.
4. The study of this peptide in the blood serum of adolescent athletes showed an increase in neopterin by an average of 3.6 times relative to the indicators of the comparison group, which is synthesized by mononuclears and macrophages in response to their stimulation by gamma interferon. Gamma interferon is a type 2 immune interferon, the production of which is activated during cytotoxic effects – viral infections.

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