STREPTOCOCCUS PNEUMONIAE: EPIDEMIOLOGY, DEVELOPMENT OF ANTIMICROBIAL SUSTAINABILITY AND EFFECTIVENESS OF VACCINATION

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Annotations: Streptococcus pneumonia (S. pneumonia) is a significant causative agent of various infections, including pneumonia, meningitis, and otitis media, particularly affecting children and older adults.The document discusses the prevalence of pneumococcal carriage, which is highest among children in preschool institutions, and highlights the impact of living with children on carriage rates.It outlines the decline in rates of penicillin-resistant strains in the USA over time but notes the emergence of certain resistant strains, such as typesetter 19A and 35B. Mortality rates associated with invasive pneumococcal diseases (IPD) vary by age and region, with higher rates observed in developing countries. The effectiveness of pneumococcal vaccination, particularly with conjugate vaccines like PCV-7 and PCV-13, in reducing the incidence of pneumococcal diseases is discussed.Risk factors for pneumococcal diseases and antibiotic resistance include previous antibiotic therapy, age, immunodeficiency conditions, and overcrowding in institutions. The document underscores the importance of ongoing surveillance for new pneumococcal strains and the development of vaccines with expanded coverage.

Keywords:Streptococcus pneumonia, Epidemiology, Antimicrobial resistance, Vaccination, Pneumococcal diseases, Carriage rates, Antibiotic resistance, Invasive pneumococcal diseases (IPD),Mortality rates, Vaccine effectiveness

Streptococcus pneumonia (S. pneumonia, pneumococcus) is one of the common causative agents of community-acquired pneumonia, meningitis, bacteria in children and adults, and acute otitis media in children. Diseases caused by S. pneumonia are divided into invasive and non-invasive according to the severity criterion. Invasive pneumococcal diseases (IPD) include: bacteria, meningitis, pneumonia and other pathological conditions in which the pathogen is isolated from usually sterile organs and tissues (blood, cerebrovascular fluid, less commonly synovial, plural or pericardial fluid). IPD often affects children under 2 years of age and adults over 60 years of age, as well as people with immunodeficiency conditions. Among non-invasive forms of the disease, upper respiratory tract infections (middle otitis, para nasal sinusitis), lower respiratory tract (bronchitis), as well as other relatively rarely recorded infections (conjunctivitis, peritonitis, arthritis, poly arthritis, etc.). [1,6,8]According to WHO, about 1.6 million people die from IPD every year, including 1 million children under 5 years of age. Vaccination of children with the seven-valet pneumococcal conjugate vaccine (PCV-7), which began in 2000 in Europe and the USA, has led to a decrease in the incidence of pneumococcal meningitis, pneumonia, bacteria and acute otitis media. It is important to note that with the beginning of vaccination

of children against pneumococcal infection, a decrease in IPD was also observed among adults.Pathogenesis of diseases caused by S. pneumonia.

When infected, pneumococci primarily colonize the pharynx. The pharynx is the primary niche for infection by S.pneumonia.[2,3,10]The outcome of colonization is the elimination of bacteria, carriage for several months, or penetration into other organs. Penetration of the pathogen into the lower respiratory tract or other parts of the body can lead to the development of invasive pneumococcal disease. The rate of pharyngeal carriage is high among children. Risk factors for the development of pneumococcal carriage are age under 6 years, large families, and attendance at children's organized groups. In adults, carriage can be triggered by cigarette smoking, asthma and acute respiratory infections. [4,5,9] According to expert estimates, the carriage rate of pneumococci increases during the first year of life, reaching 15% . It is especially high in preschool institutions. When examining children in 19 cities of the Russian Federation, carriage of pneumococci in 80 kindergartens was 49.3%, and in some up to 50.7%. In elementary school, the carriage rate of pneumococcus decreases to 35%, in high school to 25%. Adults living with children have higher carriage rates (18–29%) than those living without children (6%) .The outcome of colonization depends on the virulence of pneumococci and the state of the immune system. The penetration of pneumococci from the mucous membranes of the oral cavity and upper respiratory tract into the distal sections is prevented by anatomical barriers (the virtuosity of the respiratory tract, which makes it difficult for the pathogen to penetrate into the lungs; the epiglottis, which protects the airways from aspiration, cough reflex, sticky layer of mucus) , cilia of the respiratory epithelium), as well as cellular and humeral factors of immunity. Nonspecific mechanisms of local immunity, including the presence of other microorganisms in the pharynx, significantly limit the proliferation of pneumococcus. Pneumococcal diseases often develop after a viral infection of the respiratory tract, which affects the cilia ted epithelium and reduces its activity, and also suppresses the activity of alveolar macrophages. Airway secretions can delay the process of phagocytes . [1,5,7]

In tissues, pneumococci begin to multiply and spread through the flow of lymph and blood or through contact from the site of infection. The severity of the disease is determined by the virulence of the pathogen, its quantity, especially during bacteria, and the state of reactivity of the microorganism. Increased tendency to recurrent purulent infections, among which pneumococci play a role, in patients with a removed spleen or congenital absence of it is associated with insufficient optimization of pneumococci and the absence of the filtering function of the spleen during bacteria. Pneumococcal infection develops especially often in patients with sickle cell anemia and other forms of encephalopathy due to the fact that patients lack the ability to activate SZ in other ways and fix this opinion to the cell wall of pneumococci . If one or more protective factors are violated, pneumococci can be introduced into the distal parts of the respiratory tract. When bacteria enter the alveoli, they initially attach to their wall and spread not only photogenically, but also from alveoli to alveolar (through Cohen's pores). In the

last decade, thanks to the identification of the main virulence factors of pneumococci, the molecular cellular mechanisms have been largely deciphered development of pneumonia. In individuals with normal immune defenses, the risk of developing IPD increases with alcohol abuse, during an epidemic of influenza, diabetes, asthma, and cigarette smokers. Also, the risk of developing IPD increases among patients with primary and secondary immunodeficiency conditions (sickle cell anemia, HIV infection, cancer, splendid, organ transplant recipients). In HIV infection, risk factors for the development of pneumococcal pneumonia are tobacco smoking, drug use, CD4 cell count less than 200 cells/ml, old age and alcohol abuse. Frequent development of pneumococcal resistance to penicillin and co-matrimonial in HIV-infected people is probably associated with long-term use of these drugs for prophylactic purposes .

The bacteriological method for identifying pneumococcus remains the “gold standard” in the diagnosis of pneumococcal infections. However, the rate of isolation of pneumococcal culture by bacteriological method is low, especially in patients who received antimicrobial drugs before taking the material. This test can be used in conjunction with the bacteriological method, because may be positive even with a negative culture if the patient received antibacterial drugs before the study.

Risk factors for deaths in invasive pneumococcal diseases.

Results and discussion

Mortality from bacterial pneumonia of pneumococcal etiology varies from 10 to 30% in adults and less than 3% in children . Death rates for meningitis in adults are 16-37% and from 1 to 3% in children. The disease in this category of patients occurred with the involvement of several lobes of the lungs in the pathological process, septic shock, the need for artificial ventilation of the lungs or intensive therapy. An analysis of the clinical forms of more than 18,000 patients with IPD in Denmark revealed that the development of invasive forms of pneumococcal diseases is associated with age and the incidence of influenza . Mortality rates were as follows: 3% of cases were aged less than 5 years, 14% were 5-65 years old, and 24% were aged 65 years or older. In developing countries, mortality rates are high and reach 10-40% . In the development of drug resistance in S. pneumonia, the dominant risk factor is previous use of antibiotics. Risk factors for the development of penicillin resistance of pneumococci when carrying S. pneumonia are previous antibiotic therapy, age under 5 years, and visits to preschool and other institutions. Risk factors for the development of penicillin resistance of pneumococci in IPD are also previous antibiotic therapy, frequent acute respiratory infections, HIV infection, chronic lung diseases, and secondary immunodeficiency states. In addition, the spread of transmission of resistant strains of S.pneumonia from pneumococcal carriers.This is facilitated by overcrowding of

the population, for example, in preschool institutions, hospitals, and places of detention. Reducing the use of antibiotics may lead to a reduction in the spread of antibiotic resistance in pneumococci. The development of pneumococcal resistance to macrology antibiotics is also increasing following penicillin resistance. In the future, but pneumococcal stereotype 6C was responsible I am not in favor of increasing the number of IP D's in the USA, while time when there was a decrease in the incidence of IPD caused by stereotype 6A. In Korea, increased identification of IPD caused by multi drug-resistant mi strains of typesetter not included in the vaccine (19A and 6A), were noted before the introduction PCV7 vaccine. In 2007, weather-resistant action of antibiotics S.pneumonia (polyester-stent strain) isolated from a sick child with acute otitis media. Capsular transformations formations can form multi drug-resistant pneumococcal strains of invasive phenotype with high virulence. The frequency of detection of antibiotic-resistant pneumococcal strains varies significantly depending on the geographic region and changes over time. In the USA, a review of the results of 41 medical centers showed a decrease in rates of penicillin-resistant strains (MIC ≥ 2 mg/ml) from 21.5% in 1999-2000. to 14.6% in 2004-2005, resistance to erythromycin remained unchanged . However, the distribution of penicillin-resistant typesetter since 1999-2000. until 2004-2005 changes. There is a predominance of the penicillin-resistant strain of typesetter 19A (from 1.5% increased to 35.4%), typesetter 35B (from 1.2% increased to 12.5%), while most typesetter included in PCV7 (23F, 9V, 6V, 14) began to be detected less. A study of cultures isolated from IPD in children 2–4 years of age in Alberta and Canada showed a decrease in the detection of antibiotic-resistant strains between 2000 and 2006. This decline is was the result of a reduction in IPD due to the introduction of the PSV7 vaccine.

Pneumococcal vaccines

Vaccines have been used to prevent pneumococcal disease for more than 30 years. Several types of pneumococcal vaccines are currently in use: 23-valent pneumococcal polyacrylamide vaccine (PPV23), which has been available since 1980, pneumococcal conjugate vaccines, available on the market since 2009 (10-valent (PCV10)) and 13-valent (PCV13)) and 7-valent conjugate vaccine. Pneumococcal polyacrylamide vaccines are associated with little or no carcinogenicity in children <2 years of age necessary to induce immune memory in response to booster vaccination. The definition of “pneumococcal conjugate vaccine” is used for vaccines based on the chemical combination of S. pneumonia polyacrylamide with an immunologic protein carrier. This enhances the antibody response and induces immune memory . Re vaccination is usually not recommended for individuals with a normally functioning immune system, but single or double booster vaccination is practiced for individuals with impaired immune systems . In some high- and middle-income countries, PPV23 is

recommended for use in populations at high risk of pneumococcal disease, including people over 65 years of age.In summary, the currently available RSV vaccines are safe and effective, and the increasing number of typesetter present in these vaccines compared with the first licensed PCV7 vaccine represents a significant advance in disease control. - and mortality from pneumococcal infection in the future, especially in developing countries . WHO recommends the widespread inclusion of RSV vaccines in childhood immunization programs. Particularly in countries with high childhood mortality (i.e., for children under 5 years of age with a rate greater than 50:1000), the introduction of these multi component RSV vaccines should be a high priority. Use of pneumococcal vaccine should be considered as an additional opposition to other countermeasures with pneumonia, such as the corresponding case management, breastfeeding encouragement feeding the baby during the first 6 months -life expectancy and reduction of known risk factors.

Conclusion

Globally, mortality from invasive pneumococcal diseases is estimated at 1.6 million people annually. The risk of developing IPD is high at the age of under 5 years and over 60 years, as well as in persons with a burdened premodifier background and various immunodeficiency. Only a small number of pneumococcal typesetter are responsible for cases of IPD worldwide. In addition, the increase in antimicrobial resistance of pneumococci depends on the overuse of antibiotics and the spread of several international (pandemic) antibiotic-resistant clones One of the ways to reduce the development of antibiotic resistance in pneumococci is the targeted use of antimicrobial drugs. However, the emergence of multi resistant clones in some regions remains problematic.

Today, the optimal measures to prevent pneumococcal infection are monitoring the formation of new typesetter and the development of new vaccines with expanded coverage and carcinogenicity . So, in our republic, the expert technical group on immunization at the Ministry of Health of the Republic of Uzbekistan, according to the multi-year immunization plan of the Republic of Uzbekistan, has been planning the introduction of pneumococcal vaccine in our country since 2015. Of course, vaccinating high-risk individuals (children and the elderly) reduces the incidence of IPD. However, the duration of the effect of vaccination, the distribution of typesetter and the extent of the formation of antibiotic resistance remain not fully studied. Thus, the prevalence and diversity of diseases caused by pneumococci, their ability to develop resistance to antibiotics, which significantly reduces the effectiveness of therapy, the potential for the development of new approaches to the prevention and treatment of pneumococcal infections using modern methods diagnostics.

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