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FACTORS OF HIGH MORTALITY IN SEVERE COVID-19 PATIENTS

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✓ ***Resume***

The viability of SARS-CoV-2 at environmental facilities is maintained for up to 3 days. The transmission coefficient, i.e. the average number of people who are sure to get infected from one infected person in a population that has never encountered a particular disease before, is 1.5-2.5. The transmission routes of SARS-CoV-2 are airborne, contact and possibly fecal-oral. COVID-19 disease is caused by a new virus, so people of all age categories are susceptible to infection. The analysis conducted by the Chinese Center for Disease Control and Prevention showed that among 72,314 cases, 87% were aged 30 to 79 years, children 9 years and younger - 1%, children and adolescents aged 10 to 19 years - 1%, elderly people aged 80 years - 3%. Cases of children's disease were more often reported in the family or as a result of contact with an infected person.

Keywords: respiratory infection, stable immune response, prognostic significance

COVID-19 BO'LGAN OG'IR BEMORLARDA YUQORI O'LIM XAVFI OMILLARI

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✓ ***Rezyume***

SARS-CoV-2 ning atrof-muhit obyektlarida yashovchanligi 3 kungacha davom etadi. Yuqtirish koeffisienti, ya'ni ilgari hech qachon aniq kasallikka duch kelmagan populyatsiyada bitta kasallangan odamdan albatta yuqadigan odamlarning o'rtacha soni 1,5-2,5 ni tashkil qiladi. SARS-CoV-2 yuqish yo'llari havo-tomchi, kontakt va najas-og'iz orqali bo'lishi mumkin. COVID-19 kasalligi yangi virusdan kelib chiqadi, shuning uchun barcha yoshdagi odamlar infektsiyaga moyil. Xitoy Kasalliklarni nazorat qilish va oldini olish markazi tomonidan o'tkazilgan tahlil shuni ko'rsatdiki, 72 314 ta holatning 87 foizi 30 yoshdan 79 yoshgacha bo'lganlar, 9 yosh va undan kichik bolalar – 1 foizi, 10-19 yoshli bolalar va o'smirlar – 1 foizi. , keksa odamlar. 80 yoshda - 3%. Bolalarda kasallik holatlari ko'proq oilada yoki kasal odam bilan aloqa qilish natijasida qayd etilgan.

Kalit so'zlar: respirator infeksiya, stabil immun javob, prognostik ahamiyati.

ФАКТОРЫ ВЫСОКОЙ СМЕРТНОСТИ У ТЯЖЕЛЫХ ПАЦИЕНТОВ COVID-19

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✓ ***Резюме***

Жизнеспособность SARS-CoV-2 на объектах окружающей среды сохраняется до 3 суток. Коэффициент передачи, то есть среднее количество людей, которые обязательно заразятся от одного инфицированного человека в популяции, никогда ранее не сталкивавшейся с конкретным заболеванием, составляет 1,5-2,5. Пути передачи SARS-CoV-2 - воздушно-капельный, контактный и, возможно, фекально-оральный. Болезнь COVID-19 вызывается новым вирусом, поэтому инфицированию подвержены люди всех возрастных категорий. Анализ, проведенный Китайским центром по контролю и профилактике заболеваний, показал, что из 72 314 заболевших 87% приходились на возраст от 30 до 79 лет, дети 9 лет и младше - 1%, дети и подростки в возрасте от 10 до 19 лет - 1%, люди пожилого возраста. в возрасте 80 лет - 3%. Случаи заболевания детей чаще регистрировались в семье или в результате контакта с инфицированным человеком.

Ключевые слова: респираторная инфекция, стабильный иммунный ответ, прогностическое значение.

Relevance

The number of cases of men and women was 51.0% and 49.0%, respectively. The incidence of the disease among contact persons reached 1- 4.8%. Infected medical workers accounted for 4% of the total number of cases. The average incubation period, after which the clinical picture of acute respiratory infection (ARI) of varying severity developed, was 6.4 days (1-10 days). The average mortality rate for COVID-19 at the beginning of the pandemic reached 3.4% (for comparison: with MERS - 34.4%, with SARS - 9.6%), and then gradually decreased to 2.2%. Severe course of the disease occurred in 14.0% of cases, and the mortality rate reached 13.4%. The recovery of COVID-19 patients occurred within 2-6 weeks [6].

The results showed that out of 1,797 people who recovered from SARS-CoV-2 infection, 1,107 out of 1,215 examined (91.1%) were seropositive; the titers of antiviral AT, determined by two pan-Ig assays, increased within 2 months after diagnosis using qPCR and remained on a plateau for 4 months of the study. Among 4,222 people quarantined after contact with SARS-CoV-2 patients, 2.3% were seropositive, and among 23,452 people for whom such contact was not known, 0.3% was. Statistics showed that 0.9% of Icelanders were infected with SARS-CoV-2, and 0.3% of this infection was fatal. In Iceland, the diagnosis was confirmed by qPCR in 56% of cases of infection with SARS-CoV-2 infection. The infection was not diagnosed using qPCR (or a positive result was not obtained during testing) in 44% of people infected with SARS-CoV-2, including 14% who were quarantined and 30% who were out of quarantine [1,6].

An analysis of the survival rate of 44,672 patients with confirmed COVID-19 conducted by the Chinese Center for Disease Control and Prevention showed that male sex, old age, as well as leukocytosis and high levels of lactate dehydrogenase (LDH), heart damage, hyperglycemia and the use of high doses of corticosteroids had a direct relationship with mortality in severe COVID-19. In severe cases of the disease, arterial hypertension (38.7% and 22.2%; p=0.0001), DM (19.3% and 11.1%) were detected in hospitalized patients more often than in moderate cases%; p=0.009), coronary heart disease (CHD) (10.4% and 2.2%; p=0.0001), chronic obstructive pulmonary disease (4.8% and 1.4%; p=0.026) [3].

When PRRs is activated, downstream signaling cascades trigger cytokine secretion. Among them, interferons (interferon, IFN) of type I/III and other cytokines, such as pro-inflammatory tumor necrosis factor-α (tumor necrosis factor, TNF-α) and interleukin (interleukin, IL) 1, IL-6 and IL-18, are considered the most important for antiviral protection. Together, they induce antiviral programs in target cells and potentiate an adaptive immune response. If IFN-I is present at an early stage and properly localized, it can effectively limit SARS-CoV-2 infection]. Early evidence has been obtained that the SARS-CoV-2 virus is sensitive to the action of IFN-I/III in vitro, possibly to a greater extent than SARS-CoV-1. Using a model of intestinal epithelial cells, it was found that SARS-CoV-2 viral infection caused a stable immune response, where the reaction mediated by type III interferon was significantly more effective in controlling the replication and spread of the virus compared to IFN-I . However, the specific IFN-stimulated genes that mediate these protective effects are still being studied. It has been shown that the E locus of the lymphocytic antigen complex 6 (LY6E) prevents membrane fusion mediated by the spike protein SARS-CoV-2 (S). It is assumed that proteins of the IFN-induced transmembrane family inhibit the penetration of SARS-CoV-2, as previously shown for SARS-CoV-1. Since these cytokines represent the main barrier to viral infection, coronaviruses have developed several mechanisms for inhibiting the induction and transmission of IFN-I signals. Coronaviruses inhibit the release of type I/III IFN from infected cell lines, primary bronchial cells, especially in severe COVID-19 compared to mild or moderate cases. Coronaviruses counteract at every stage of the pathway - from PRR perception and cytokine secretion to IFN signal transduction and avoid PRR activation or complicate their recognition [4].

T cells play a fundamental role in viral infections: CD4 T cells provide B-cell assistance for the production of AT and control the response of other immune cells, whereas CD8 T cells kill infected cells to reduce the viral load. Proper management of COVID-19 patients requires a better understanding of the pathogenesis of the disease. Sudden clinical deterioration 7-8 days after the onset of the first symptoms of the disease indicates that severe respiratory failure (DN) in COVID-19 is due to a unique pattern of immune dysfunction. A study of the immune responses of 54 patients with COVID-19 revealed that 28 of them had severe DN and macrophage activation syndrome or very low expression of human leukocyte antigen D (HLA-DR), accompanied by

deep depletion of CD4, CD19 and NK lymphocytes [2,4].

The reaction of B cells to the virus serves not only to protect against initial exposure, but also to provide enhanced immunity against reinfection. After the infection resolves, plasma cells formed in the acute and convalescent phases continue to secrete AT, causing serological memory. Memory B cells, which are also formed during primary infection, make up the second arm of B-cell memory. Memory B cells can quickly respond to reinfection by generating new high affinity plasma cells. Long-term protection is achieved through the induction of long-lived plasma cells and memory B cells. There is great interest in understanding the lifetime of B-cell memory responses to SARS-CoV-2. Protection from reinfection has direct medical and social consequences, as the whole world is developing vaccination strategies to resume normal activities. In patients with COVID-19, data on universal seroconversion and the absence of significant signs of reinfection indicate stable AT production, which, along with the response of memory T cells, will protect against reinfection. Due to the limited time period of the outbreak of this infection, it is not yet possible to know the nature and extent of the reaction of long-term memory [5].

This phenomenon is observed when virus-specific IgGs that do not neutralize facilitate the penetration of viral particles into Fc receptors of expressing cells, in particular macrophages and monocytes, which leads to the activation of these cells. At the moment, there is no evidence that naturally produced SARS-CoV-2 AT-tics contribute to the development of pathological signs that are observed in COVID-19. However, this possibility should be taken into account when it comes to experimental design and development of therapeutic strategies. It is important to note that in all descriptions of ADE related to coronavirus, FcR was necessary to trigger AT-mediated pathology. High doses of intravenous immunoglobulin (IVIG), which can reduce ADE, have been tested in patients with COVID-19 [4].

Serological markers of routine blood analysis were obtained by comparing patients with mild/moderate symptoms and patients with severe symptoms. These are various proteins of the acute phase of inflammation, such as serum amyloid protein and C-reactive protein (CRP), an increase in the level of which is unique for patients with COVID-19 compared to other viral infections. Other constantly recorded markers in those who died from infection include elevated levels of procalcitonin, IL-6, urea, creatinine, cystatin C, direct bilirubin and cholinesterase in the blood serum. Inflammatory markers are often found in severe cases of COVID-19 and may be related to the severity of symptoms and clinical outcome.

During the incubation period and the early phase of the disease, the number of leukocytes and lymphocytes is normal or slightly reduced. After SARS-CoV-2 binds to overexpressing ACE2 organs, such as the gastrointestinal tract and kidneys, an increase in nonspecific markers of inflammation is observed. In more severe cases, there is a pronounced systemic release of inflammatory mediators and cytokines with a corresponding increase in lymphopenia and potential damage to lymphoid organs. Lymphopenia, increased proinflammatory markers and cytokines, hypercoagulation of blood characterize severe cases of COVID-19 with signs of cytokine release syndrome and are associated with a variety of clinical manifestations from mild to severe and critical. Most of the serological and immunological parameters observed in COVID-19 are associated with the severity of the disease, but may not have prognostic significance, since they are not effective for early detection of patients at higher risk. A number of risk factors for the severe course of COVID-19 have been established, among which the patient's age and comorbidity are of leading importance - factors determining the prognosis of nosocomial mortality in hospitalized patients [3.5].

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