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A review of detection, treatment and prevention of COVID-19

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ABSTRACT: As one of the serious infectious diseases, COVID-19 has brought serious harm to people's health and safety, and increased the burden of family and society. The COVID-19 pandemic continues to spread around the world. This article mainly introduces the case characteristics, detection methods, treatment methods, vaccine development and prevention methods of COVID-19.

Keywords: COVID-19, nucleic acid testing, inhibitors, vaccines

I. INTRODUCTION

Corona Virus Disease 2019, named by the World Health Organization as "COVID-19", refers to pneumonia caused by novel Coronavirus 2019 infection. Because of its high infectivity and deadly nature, much research has been done on COVID-19[1-2]. Laboratory characteristics of the COVID-19 include normal or reduced white blood cell count and reduced lymphocyte count in the early stages of the disease; some patients showed increased sidase, myoglobin and myoglobin. In most patients, c-reactive protein and esR were elevated and procalcitonin was normal. In severe cases, D- dimer increased and peripheral blood lymphocytes decreased gradually. Chest effects showed multiple small patchy shadows and interstitial changes in the early stage, especially in the outer lung zone, and then developed into multiple ground glass shadows and infiltrating shadows in both lungs. Severe cases can appear lung consolidation, pleural effusion is rare. The clinical manifestations were fever, fatigue, dry cough, nasal congestion, runny nose and other upper respiratory symptoms were rare. Half of the patients developed dyspnea more than a week later; Severe cases rapidly progress to acute respiratory distress syndrome, septic shock, refractory metabolic acidosis and coagulation dysfunction. It is worth noting that severe and critically ill patients may have moderate to low fever in the course of disease, or even no obvious fever; Some patients have mild onset symptoms, but no fever, most recover after a week, most patients have a good prognosis, a few patients are critically ill, or even death. Tens of thousands of people have died from acute respiratory infections caused by Novel coronavirus infections[3]. In this paper, we mainly introduce the case characteristics, detection methods, treatment methods, vaccine development and prevention methods of COVID-19.

II. COVID-19 VIRUS TESTING

There are three methods to detect COVID-19 virus: nucleic acid test, antigen test and antibody test. Nucleic acid test samples are nasopharyngeal swabs, sputum and other lower respiratory tract secretions, blood, feces, etc. Novel coronavirus is sensitive to ULTRAVIOLET light, heat, partial disinfectants, such as, 75% ethanol, ether, chlorine-containing disinfectants, peracetic acid and chloroform, all of which can effectively inactivate the virus. Improper transportation and storage can easily lead to degradation, and improper selection of sample tube and preservation solution can easily lead to false negative nucleic acid test results. Trizol method was used to extract RNA; viral RNA is reversely transcribed into cDNA; PCR amplification; results analysis.

Antigen detection is a double antibody clip ELISA principle, the sample drops on the sample pad, through liquid chromatography through the binding pad, NC film on the detection line (T line) and quality control line (C line). The binding pad contains labeled antigen-specific antibodies that bind to the antigen (viral protein) in the sample. When the flow reaches the test line (T line), a second antigen-specific antibody fixed to this line rebinds to the antigen and will present a positive result. The 2019-N Co Vnovel Coronavirus antigen detection reagent based on colloidal gold immunochromatography and the Novel Coronavirus protein rapid detection and detection kit based on nanoparticle chromogenic technology and double antibody sandwich.

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The principle of antibody detection is colloidal gold immunotechnique, in which colloidal gold labeled recombinant novel coronavirus antigen and quality control antibody gold markers are sprayed on the binding pad. Two detection lines (G line and M line) and one quality control line (C line) are coated on the NC membrane. Line M was coated with mouse anti-human IgM monoclonal antibody, line G was coated with mouse anti-human IgG monoclonal antibody, and line C was coated with quality control antibody. When the sample is added to the well, the sample is moved forward along the test card by chromatography, and if the sample contains COVID-19 IgM antibody, the antibody binds to the colloidal gold labeled virus antigen to form a sandwich complex, which will give a positive result. If the sample contains novel Coronavirus igg antibody, the antibody will bind to the colloidal gold labeled Novel Coronavirus antigen to form a sandwich complex, which will result in a positive result. The card also contains a quality control line (C line) to determine if the chromatography process is smooth. The difference among Nucleic acid detection, antigen detection and antibody detection is seen in table 1.

Table1:Nucleic acid detection, antigen detection, antibody detection

Test Method	Test target	Test sample	Application scenario
nucleic acid testing	Virus genes (RNA)	Nasopharyngeal swab, pharyngeal swab, nasal swab, sputum, bronchial lavage fluid, alveolar lavage fluid, etc	It is used for diagnosis in medical institutions and laboratories
antigen test	Viral protein (N protein or S protein)	Nasopharyngeal swab, oropharyngeal swab, nasal swab	It is used for rapid screening of high-risk individuals and rapid population shunting
antibody test	IgG and IgM antibodies	Blood samples; Serum, plasma and whole blood	medical institutions and laboratories

III. TREATMENT OF COVID - 19

Now people treat COVID-19 by stopping the virus from entering, stopping the virus from being released, and stopping the virus from replicating[4-5]. Block virus entry uses ACE2 inhibitors, transmembrane Serine protease (TMPRSS2) inhibitor, ACE2 analogue (binding S protein), S protein inhibitors. Its principle is the protein mediated by virus entering cells →ACE2, TMPRSS2; inhibit related proteins and prevent the virus from entering. The approved drugs are entzatovir and preitovir. Side effects during treatment include overmedication that breaks the balance between Ang II and ANG1-7, cause inflammation in the lungs and even pulmonary fibrosis, preventing the release of virus is mainly to inhibit the activity of ADAM17 protein, protect ACE2, prevent the occurrence of lung diseases. Nucleotide analogues can inhibit RNA replication. In addition, non-invasive ventilation is used as an adjunct to the treatment of COVID-19. Paxlovid (nematvir/ritonavir tablets) and the neutralizing antibody combination ambavitumab/romisizumab are recommended in the ninth edition of clinical Protocols.

In traditional Chinese medicine, three drugs and three prescriptions are used to treat COVID-19. Specifically, Lianhuaqingwen capsule/granule, Jinhua Qinggan granule, Xuebijing injection, and Qingfei Baidu granule, Dampness Baidu granule, and Xuanfei Baidu granule transformed from the "three" prescriptions of qingfei Detoxification soup, damp detoxification side, xuanfei detoxification side.

IV. COVID - 19 VACCINE

As of December 2020, 60 vaccine candidates have been approved for clinical trials based on 6 different technology routes, including inactivated vaccines, nucleic acid vaccines (including DNA and mRNA vaccines), vector vaccines, protein subunit vaccines, live attenuated vaccines and virus-like particle vaccines. Seven of them (3 inactivated vaccines, 2 mRNA nucleic acid vaccines and 2 vector vaccines) were approved for emergency use or conditionally marketed.

According to the research and development principle and production process, vaccines are divided into traditional vaccines and new vaccines, among which the traditional

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vaccines contain live attenuated vaccines, inactivated vaccine; toxoid vaccine. The new vaccines include subunit vaccines, peptide vaccines, vector vaccines and nucleic acid vaccines. The principle of subunit vaccine is to decompose the pathogen to obtain antigen; The principle of polypeptide vaccine is recombinant protein vaccine, synthetic antigen. Vector vaccines work by delivering antigen genes into the body via harmless microbes. The principle of nucleic acid vaccine is that the gene fragment of pathogen immunogen and plasmid vector are injected into the host body.

The vaccine production process involves four steps. First, a sample of the virus is taken from a patient's body. Step two, isolate the virus and make a vaccine. In this step, the traditional vaccine is to select the most suitable virus after inactivation, attenuated and other treatment into the vaccine, nucleic acid and viral vector vaccines, on the other hand, sequence the virus's genes to find the key target, and make a protein or part of it into a candidate vaccine. The third step, animal experiments are divided into two steps, first we inject vaccine for the test animals and observe, blood test, evaluation of the safety and effectiveness of the vaccine; after that, animal protection tests are carried out to attack vaccinated animals with live virus and see if they become infected. Fourth step, after ensuring that the process is controllable, the quality is stable and safe and effective, the clinical trial can be applied to the National Drug regulatory department. There are three clinical trials, the first of which focuses on the safety of the vaccine in humans, usually involving dozens to 100 subjects. The second phase tested the effectiveness of the vaccine to see if it stimulated white blood cells to produce antibodies, with hundreds to thousands of participants. Phase III used a randomized, blind, placebo-controlled design to fully evaluate efficacy and safety in a larger population. After completing the above four stages, the vaccine can apply for a production license and go through procedures such as state approval, mass production and sampling inspection before it can be officially produced and marketed.

At present, there are inactivated vaccines, nucleic acid vaccines and vector vaccines. The principle of inactivated vaccine is that after the virus is amplified and cultured, the whole virus with infection is inactivated by physical or chemical methods, so that it loses its virulence and retains its immunogenicity. The advantages are that the inactivated vaccine can increase the immunogenicity by adding adjuvants, and it has the advantages of simple production process, mature preparation and industrialization technology platform, good stability, safe use, controllable quality standard and so on. The disadvantage is that it needs to increase the number of inoculants to maintain the immunogenicity, and the biosafety level in the inactivation process and production process is higher. Effect: After 2 doses, all patients developed high titer antibodies, the positive conversion rate of neutralizing antibodies was 99.52%, and the protective efficacy against COVID-19 was 79.34%

Nucleic acid vaccine includes DNA vaccine and mRNA vaccine. Its mechanism is to construct DNA plasmid or mRNA fragment in vitro as the immunogen, which is injected by plasmid or introduced into the human body by making mRNA nanoparticles to synthesize protein antigen in vivo and induce the body to produce immune response. The advantages of acid vaccine are low risk of transmission of exogenous factors, rapid and flexible construction, easy mass production, low production cost, but there are risks of integration into the body's own nuclear DNA (DNA vaccine), easy degradation, storage and transportation temperature requirements (mRNA vaccine) and other disadvantages. Effect: Two PHASE iii clinical trials of NOVEL coronavirus RNA vaccines were announced in the United States to meet the endpoint requirement of primary efficacy, with protective efficacy of 94.1% and 95.0%, respectively

Vector vaccines are constructed by embedding protective antigens into other specific viral or bacterial vectors (such as adenoviruses, influenza viruses, salmonella, etc.). The advantages of vector vaccine are rich in vector sources, easy to produce and prepare, can stimulate humoral immunity and cellular immunity at the same time, the dosage is small, the immunogenicity is close to natural, and the vector itself can play an adjuvant effect; However, the presence of vector virus - related antibodies in human body has certain influence on the inoculation effect. Effect: The phase ii clinical trial of the non-replicating adenovirus vector vaccine in China showed that after 28 days of full dose and half dose inoculation, the positive conversion rate of RBD antibody to the RBD region of virus S protein was 96% and 97%, respectively.

Other vaccines include protein subunit vaccines, live attenuated vaccines, and virus-like pellet vaccines. Protein subunit vaccine constructs the target antigen gene of the virus on the expression vector through recombination, and then transforms into the cells of bacteria, yeast,

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mammals or insects, induces the expression of antigen protein, and makes the vaccine after purification. Live attenuated vaccine is used to treat the pathogen and mutate it. Weakened or even non-toxic pathogen variants are obtained through subculture, and immunogenicity is retained. The live virus variants are inoculated into the human body, which will not cause disease, but can induce immune response. Virus-like particle vaccines are highly structured hollow particles composed of one or more capsid proteins of the virus that are self-assembled in a heterologous system and have the same or similar structure as natural virions, but do not contain the genetic material of the virus.

Inactivated vaccine and protein subunit vaccine won't cause infection, and live attenuated need to replicate in the body, there is virulence reversion or the risk of transmission of infection, so the inactivated vaccine and protein subunit vaccine safety than live attenuated, protein subunit vaccine composition more precisely, security is slightly higher than the inactivated vaccines. DNA vaccine in nucleic acid vaccine has the risk of oncogene activation, or tumor suppressor gene inactivation, or chromosome instability caused by the integration of foreign DNA into the host genome. The synthetic materials and wrapping materials used in the synthesis of mRNA vaccine may be toxic and have the risk of inducing apoptosis of surrounding host cells. Non-replicating adenovirus vector vaccines cannot self-replicate and are safe. However, due to the wide range of adenovirus infection and lack of targeting, adenovirus vectors may infect other normal tissue cells while infecting target organs and cells, resulting in adverse reactions.

In its target product description for COVID-19 vaccines, WHO states that the protective efficacy of COVID-19 vaccines is required to be at least 50%, and that efficacy can be assessed based on the endpoint of "disease, severe illness and/or detoxification/transmission capacity". Among the four vaccines whose efficacy has been announced so far, the protective efficacy of inactivated vaccine reached 79.34%, carrier vaccine 62% ~ 90% and mRNA vaccine more than 90%, all meeting the requirements. The meaning of vaccination is herd immunity.

V. COVID-19 SEQUELAE AND PREVENT

Fatigue (58 percent), headache (44 percent), attention deficit (27 percent), hair loss (25 percent), and breathing difficulties (24 percent) were the five most common after-effects of COVID-19. Other symptoms include lung disease (cough, chest discomfort, reduced lung dispersion, sleep apnea, and pulmonary fibrosis), cardiovascular disease (arrhythmia, myocarditis), and neurological and psychiatric disorders (dementia, depression, anxiety, obsessive-compulsive disorder). Half of the patients showed decreased lung diffusion function, decreased respiratory muscle strength, and abnormal lung imaging. From the imaging results, it was found that 94% of discharged patients had abnormal lung CT images, mainly ground-glass density shadow (GGO). Abnormal lung CT images are also seen in asymptomatic patients. Fibrosis is present in about 25% of mild-to-moderate cases, and in a cohort dominated by severe cases, pulmonary fibrosis is present in about 65% of those who have recovered. At 1-year follow-up, COVID-19 infection was associated with a 63% increase in any cardiovascular outcome and a 55% increase in major adverse cardiovascular events (MACE, a composite end point for myocardial infarction, stroke, and all-cause mortality). Specifically, COVID-19 infection was associated with a 53% increased risk of cerebrovascular disease, a 69% increased risk of arrhythmias, a 102% increased risk of combined cardiac or pericardial inflammatory disease, a 66% increased risk of ischemic heart disease, a 139% increased risk of thromboembolic disease, and a 72% increased risk of heart failure. The risk of mental health event diagnosis or prescription increased by 60% in the COVID-19 group. Specifically, the COVID-19 group had a 35% increased risk of anxiety, 39% increased risk of depression, 38% increased risk of stress and adjustment disorders, 55% increased risk of using antidepressants and 65% increased risk of using benzodiazepines. In addition, the COVID-19 group had an 80 percent increased risk of cognitive impairment and a 41 percent increased risk of sleep disorders.

Possible causes of COVID-19 sequelae include: cell or tissue damage directly caused by novel coronavirus infection; chronic inflammation caused by potential reservoir or non-infectious novel coronavirus fragments; chronic COVID-19-related immune depletion; Virus-induced autoimmunity; Abnormal immune metabolism and mitochondrial dysfunction; An imbalance of the renin-angiotensin system (RAS).

In daily life, we should maintain good personal and environmental hygiene, balance nutrition, proper exercise, adequate rest, and avoid excessive fatigue, improve health literacy, develop "one meter noodles", wash hands frequently, wear

masks, chopsticks and other health habits and lifestyle, sneeze or cough should cover the mouth and nose. In addition, we should keep indoor ventilation good, scientific personal protection, respiratory symptoms should be timely to the fever clinic for medical treatment. Those who have recently been to high-risk areas or have contact history with confirmed or suspected cases should take the novel coronavirus nucleic acid test on their own initiative[6].

VI. CONCLUSION

In this paper, we mainly introduce the case characteristics, detection methods, treatment methods, vaccine development and prevention methods of COVID-19, which is more conducive to understanding and mastering COVID-19

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