The Three COVID-19 Treatments: Vaccine, Antibody, And Inhibitor

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Abstract. Coronavirus disease (COVID-19) as a severe contagion induces the international public health emergency. Millions of people have been infected or died. The whole society affected because of the suspending of work. To deal with this situation, scientist did studies and research on various kinds of treatments. Among those, vaccine, antibody and inhibitor are three common treatments for COVID-19. Vaccines, by mimicking the infection of external pathogens but with lower pathogenicity, help the host establish long-term protection, which is the key prophylactic strategy. Antibody, the product of immune response, is taken as the treatment after infection. Inhibitor, usually small molecules or enzymatic analogues, aims to interfere with the functions of viral enzyme and disrupt the life cycle of virus. In this review, we conducted a thorough investigation by literature reviewing, illustrating the definition, components and mechanisms of these three treatments, besides, some specific approved drugs in the corresponding categories are also presented.

Keywords: antibody, COVID-19, inhibitor, treatment, vaccine.

1. Introduction

In December the 31st of 2019, news about a cluster of unexplained cases of pneumonia was first reported by the health commission of China's Hubei province. The World Health Organization named the disease as Coronavirus disease 2019 (COVID-19) [1]. It turned into an outbreak and led to an international public health emergency. COVID-19 is a contagious viral illness spreading through the direct or indirect contact with the infected person. The typical virus exposure approaches are spreading through coughing and sneezing, or the liquid contacting with mouth and eyes. Being a systemic disease, COVID-19 uses the blood-base transmission, effecting various kinds of organs in addition to lung. Hence, COVID-19 can caused an enormous scale of acute threat to human's life in the whole human society.

The pathogen of the contagious viral illness, COVID-19, is the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [2]. As a type of coronavirus, SARS-CoV-2 is an RNA virus with the characteristic of pleomorphic, enveloped, positive-sense, and single-stranded genome. SARS-CoV-2 have plenty of similarities with other pathogens like SARS-CoV, which is the pathogen of severe acute respiratory syndrome pandemic occurred in 2003. SARS-CoV-2 shares 87.6-89% nucleotide sequence similarity with the bat-origin SARS-like coronavirus. SARS-CoV-2 contains four structural proteins: spike (S) protein, nucleocapsid (N) protein, membrane "matrix" (M) protein, and envelope (E) proteins. The construction of the four proteins decides the infectivity and toxicity of the infectious virion. SARS-CoV-2 is known as an enveloped virus which nucleic acid and N proteins are below the lipid bilayer. SARS-CoV-2 utilized the host cells' lipid to form new virion. The N protein protected the viral genome from the attacking by the host cells and depart from the viral genome before the proliferation; as new viral genome formed, N protein will repeat the process. The viral genome will use the host cell ribosomes to translate its protein. To form the lipid for virus, host lipids are repurposed for the replication. After E protein, M protein, S protein form the viral envelope and embedded into the repurposed lipid bilayer, the infected cell will bud off [3].

Generally, SARS-CoV-2 affect the epithelial tissue and respiratory system, and death cases of COVID-19 are mostly related to the respiratory distress syndrome causing by the infection of epithelium and alveolar macrophage activation in the lung [3]. Until the 31st of December 2023, the official reported death figure is 6,982,594 people [4]. As a severe contagious disease ruining the society, many scientists studied on the treatment for COVID-19. Hence, SARS-CoV-2, one of the most extensively studied virus, receive plenty of scientific publications describing the antibodies, vaccination, and inhibitors to cure [5].

2. Three Different Treatments

2.1. Vaccine

2.1.1 What is Vaccine

Vaccination is an effective method that protect people from the disease, before they contact with the virus. Vaccine triggers the immune reaction of the body for the disease. After receiving the vaccination, the natural defenses of the body will build a resistance against certain viruses, and the immune system will turn stronger. Vaccines are safe because they do not bring about disease and result in other further severe conditions. The side effects of vaccination are slight and temporary tiredness or discomfort which caused by the immune respond, such as a sore arm or mild fever. Severe circumstances have some possibilities to appear; some potential exceptions are the receiver getting allergic to specific ingredient contained in the vaccine. Inside of the vaccines are the germs in form of killed or weaken conditions. Most vaccines are administrated through needle injection; some are sprayed in mouth or nose [6, 7, 8]. Vaccination helps to prevent the disease before people touch with the virus. It is a useful preparation for people to sustain their body's health.

2.1.2 How does Vaccine work?

Vaccines make body knows how to defend the disease. The long-term impacts of infecting by a disease are unpredictable and irrevocable. The working principal of vaccine focuses on imitating the infection. Human's natural defensive system is activated; it learns how to resist the virus before the virus itself coming into the body. Antigen as an active ingredient contains in all kinds of vaccine. The most common type of antigen is the germs in form of killed or weakened condition. Other types are the small parts of the germ's exterior surface or genetic material, and bacterial toxin which has converted into non-toxic. These antigens all severe a function to intimate the appearance or actions of the virus. As the antigen enter the body, the immune system will recognize it as the invader and make the corresponding response. The body will produce the antibody to the particular disease that the antigen origins from. After all, when people encounter the complete and activated virus, the immune system will give the right response rapidly to save against the disease. People who administrated the vaccine are less likely be infected than the individuals who do not received the vaccine [6, 7, 8].

There are vaccines that require people to receive more than one shot. The shot or shots after the original vaccine, the primary dose, is called the vaccine booster. The vaccine booster served as a reinforcement for the body's protection to the virus. The immune system's memory toward the virus. If the immunity will decrease over time, the additional shot plays as a reminder for the immune system to react; it also provides the improvement on the original vaccine. People received doses in separate time. The body needs time to digest and to respond to vaccine. After the side effects are over, the next shot will implant into the body [9].

The Covid-19 vaccines work in the same principle with other vaccine. Vaccine can effectively reduce the possibility of people being infected when they are exposed to the COVID-19 virus. There are various types of vaccine that used by different technologies [10].

2.1.3 Viral Vector Vaccine

Viral vector vaccine transfers information by the harmless vector to inform the cells how to create copies of the innocuous part of the virus. Adenovirus, a double stranded-DNA virus, is a type of vaccine deliverer has early genes and late genes. Early genes can replicate the virus, and late genes can release the virus. For example, adenovirus loads the information to the cells about the instructions of producing a similar and harmless part of the disease. Encoding the isolation of SARS-CoV-2 S protein and incorporating into the adenovirus, the viruses which first grow into specialized cells and are purified become the vaccine. The copies will remain in the body and trigger the immune system to resist against the copies [8,11].

2.1.4 Messenger RNA (mRNA) Vaccine

The molecule, messenger RNA (mRNA), instructs people's body to create proteins. Body cells produce the harmless proteins which are similar to the one on the virus because of the informing of mRNA inside the virus. The protein makes the immune system to give the response. The existing of the virus will create the antibody from the immune system for the sake of protecting the body from outside invading. This kind of vaccine gives instructions to the body to manufacture part of the virus, but the virus will not lead to the disease. After all, if people are infected by the disease, the antibody will work and start fighting against with the virus [8,12,13].

2.2. Antibody

2.2.1 What is Antibody

Antibodies plays an important role in the immune system. As a disease-resisting protein, antibodies are produced by the immune system and give response to the invaders; they recognize the viruses and eliminate these harmful outsiders. Antibodies are produced by the reaction toward the infection or the vaccination that implanted the viruses into the body. Antibodies are in Y-shape that have the upper part and the base part. The two upper parts can combine with the outside invaders which are all known as antigen no matter its level of completeness. The base part can assist the interaction of the antibodies with the other parts of immune system; the base is constituted by two light and two heavy protein chains. The three-dimensional structure of the antibodies provides themselves the feature of specificity and affinity which helps to incorporate with numerous numbers of other antigens. Antigens are foreign substances inside the body, for instance viruses, bacteria, and other diverse toxins [14, 15].

Antibody is originated from, the specialized white blood cell, B cells. The interacting between antigens and B cells bring about the circumstance that B cells divide and clone themselves. As a result, the clone B cells release millions of antibodies into the human body's blood stream and lymph system. The antibody may remain in many different positions of the human body, including the skin, lung, tears, saliva and so on [14].

2.2.2 How does Antibody work?

Antibody has the molecules on surface which is different from the molecules inside of the human body. Molecules of antibody can realize the outsiders. Each antibody has a task: marking the invader for other immune cells to destroy or eliminate the invader by itself. When the antibody recognizes and combine with the antigen, the immune response triggers, and then other body systems will start to resist against the invading antigen. The resisting actions will memorize by the memory cells for antigen-producing that will exist in human body in a long period of time after the recovery. The memory cells serve the purpose of knowing how to prepare, response in a better and faster way when facing the invading antigen.

The Antibody for COVID-19 will receive after people's infection and recovery or receiving the specialized vaccine. Receiving vaccine after the infection can enhance the antibody which improve the immune responses and the protection from viruses. The lasting time of the COVID-19 antibody are still in research process. Some research results shows that the antibody will last at least 5 to 6 months after infecting by the disease. However, some research also indicates that the recovery patients have B cells that only aim at specific virus staying inside their body and remaining for plenty of years. This ensures that the human body can produce the antibody rapidly when facing the same type of virus again.

2.2.3 Convalescent Plasma

Five types of antibodies are categorized by each corresponding position inside the human body. A single letter labels each type of antibody and attach to the abbreviation of immunoglobulin (Ig); they are IgA, IgD, IgE, IgG, and IgM. IgA remains in the saliva, tears, mucus, breast milk, and intestinal fluid in the human body, preventing the pathogens coming inside by ingesting or inhaling. IgD places on the surface of the B cells. The specific function is unknown, but it is considered serving to support the maturation and activation of the B cells, according to the experts. IgE remains on the skin, lung, and mucus membranes. It leads, a type of white blood cell, mast cells releasing histamine and other chemical substances into the bloodstream of the human body. IgE may cause allergic reactions. IgG mainly exists in the blood and tissue fluid. Being the most common antibody, it occupies 70%-75% of all immunoglobulins inside the human body. IgG prevents the human body's infection from viruses and bacteria. IgM, the first line of defense against the infection, stays in blood and lymph system. It helps the immune regulations [14, 15].

One of the methods is named as convalescent plasma (CP). IgA, IgM, and IgG play important roles in making the reaction of antibody for SARS-CoV-2 effective. The high level of IgA and IgG are displayed in the severe patients; the low level of IgM is shown on the patients with no symptom. Those recovered COVID-19 patients have high-level of neutralizing antibodies. Depending on the discoveries, CP extracts the plasma from recovered COVID-19 patients and injected to the patient with severe condition [16].

2.2.4 Monoclonal Antibody

Monoclonal antibody (mAb) is produced in the laboratory instead of the human body. It intimates the ability of immune system to response and fight against the invading pathogens. These unnatural antibodies are created and exists because some individuals with weakened immune system can not receive enough protection from the vaccinations or their own antibody. Vaccinations are not able to provide ample amount of protection to oppose with the severe forms of COVID-19. Therefore, mAbs become an ideal therapeutic solution for these group of individuals [17].

Scientists take the mAbs from the single lineage of B cells. They then choose and aim at a certain antibody gene to encode. The mAbs will produce by a large scale. The treatment efficiency depends on the extent that these artificial antibodies can bind with specific target. The mAb is able to combine with the antigen part of the microorganism [17].

For COVID-19, the virus' spike proteins are target by the mAb to prevent the SARS-CoV-2 entering the human body. The combination with virus' spike proteins avoids the infection of the body cells. The mAb compromises the biological effects creating by the virus [16].

2.3. Inhibitor

2.3.1 What is Inhibitor

In Inhibitors can interact with proteins and reduce the objective's biological activities. The chemical or biological molecule from inhibitors will regulate by slowing down or blocking the chemical reactions happening. by These are categorized by their molecule structure and mechanism. Medication has diverse type of inhibitors for the medication, the classification including irreversible inhibition, reversible inhibition. Irreversible inhibition connects with enzyme by covalent bond, for the sake of inactivating the enzyme by destroying its structure and function. The reversible inhibition uses a non-covalent bond to combine with the enzyme by a reversible interaction. The enzyme can reactivate as the inhibition leaves. The reversible inhibition can divide into competitive and non-competitive inhibition. Competitive inhibition happens when the molecule similar to the actual substrate molecule bind with the active site and prevent the actual substrate molecule from binding. The non-competitive inhibition binds with the enzyme in a place other than the active site. Hence, the enzyme no longer properly fits into the substrate molecule and catalytic reactions will not happen on enzyme. The substrate molecule does not affect the result of inhibitors [18].

Small molecule inhibitor is one of the types which refers to a compound with a molecule weight less than 1000Da. It can both be found in the nature and produce in the laboratory. Small molecule inhibitors have lots of advantages because of its properties. The chemical properties inside makes its druggability performing good. It also has well spatial dispersion [18].

2.3.2 How does Small Molecule Inhibitor work?

The small molecule inhibitors have a number of applications, such as drugs, pesticides, and herbicides. When the small molecule inhibitor work as a human-used drug, it aims the human enzyme as the target and correct the pathological condition [18].

2.3.3 Azvudine

Azvudine (FNC) is China's first oral SARS-CoV-2 RdRp inhibitor. FNC is modified and improved from the HIV RdRp inhibitor RO-9187. RdRp is a conserved protein without a human equivalent. For SARS-CoV-2, it is a prospective target for the therapeutic inhibitor method. The hydrochloride salt generating from FNC makes itself having a better antiviral activity in vitro. It also shows a board-spectrum antiviral property in vitro. As a result, FNC has a better therapeutic result by oral [19, 20].

Through the cellular kinases, FNC converted into its active form, FNC-NTP, which can cease the RNA replication of SARS-CoV-2. FNC also has been proved as safeness and efficiency by the HIV cases; the cytotoxicity level is low. Hence, FNC can cause the COVID-19 patients appearing the symptom of temporary and mild dizziness; lowering the oral doses can effectively blow off the side effects. In addition, FNC has a relatively inexpensive price for patients to use [20].

2.3.4 FB2001

FB2001 is China's first inhaled aerosolized SARS-CoV-2 M^{pro} (NSP5). NSP5 is a three-domain cysteine protease that plays an important character in the replication and transcription of the virus. NSP5 inhibitor does not have a human equivalent and is a high-profiled antiviral. During the experiment, the NPS5 inhibitor exhibits strong antiviral effects in cell culture, animal model, and clinical trials. FB2001 is viewed as a prospective board-spectrum inhibitors since it can reduce the viral load in lung significantly. Furthermore, some studies demonstrate that FB2001 has a well safety, tolerance, and pharmacokinetics [20].

3. Conclusion

To address the problem that a large scale of people among the world infected by the COVID-19, vaccine, antibody and inhibitor provides people with different choices to prevent or cure this contagious disease. These therapeutic methods not only ensure the human health, but also guarantee the functioning of the society. Different treatments have different target population. Their advantages assist human to recovery their body health and the whole society.

Limitations exist in the three therapeutic strategies. For vaccine, the demand is far greater than the actual supply. In 2021, only millions of the available vaccines are provided for the few billion patients. The cost of many vaccines is expensive for the massive production of low and middle-income countries. Half-dose vaccine which reduces half of the dose and double the available dose is proposed to solve this problem. Nevertheless, the effectiveness and safety are still doubtful [21]. Different limitations are presented in different type of antibodies. CP is restricted to the patients with enough antibodies and needs large infusion volume. The mAb can used on patients with low antibodies, but it is not as effective as CP. [22, 23]. Inhibitors are not able to handle the SARS-CoV-2 variants. The concern on drug resistance makes the searching on new compound in inhibitors [24]. In conclusion, the three different treatments all have a promising future to improve the therapeutic effect and amend the side impacts.

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