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The role of vaccine in COVID-19

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Abstract. The sudden outbreak of COVID-19 in Wuhan, China, has brought sudden harm to people. Under such circumstances, many vaccines have been invented and created, and all kinds of vaccines also carry their own advantages and disadvantages. It is essential for population to understand the working principle and basic production method of each vaccine. At present, there are many vaccines for the novel coronavirus epidemic, but there are three vaccines that mainly occupy the market. Recent study has found that adenovirus vaccine is effective to safe people from the virus, but it can give people some bad symptoms. mRNA vaccines can increase the immune system after a second or multiple doses, especially in people over 40 years-old. In the meantime, recombinant protein COVID-19 vaccine has a strong immune response with stability of the vaccine immunity. In this paper, the most basic principles and the lowest logic of these vaccines are introduced respectively. In addition, these vaccines are combined with some studies on clinical symptoms. This article also analyzes the shortcomings and benefits of these different vaccines, and this review will recommend methods to avoid infection based on the structure of all COVID-19 vaccines and pathogens.

Keywords: COVID-19, Vaccine, Treatment.

1. Introduction

The World Health Organization calls it COVID-19, and the Committee on the International Classification of Viruses has named it SARS-cov2, Sars-cov-2 belongs to the β genus of coronavirus and belongs to the seventh kind of coronavirus that can infect humans. Its genetic characteristics are significantly different from SARS-CoV and MERS-CoV, which can cause SARS-cov infection. And there also should mention that this is because coronavirus have similar a heritage of SARS-cov.so that's why named the virus SARS-cov2.At present, there are seven known coronaviruses that infect humans, which are HCoV-229E, HCoV-OC43, SARS-CoV, HCoV-NL63, HCoV-HKU1, MERS-CoV and SARS-CoV-2 [1]. Following then, the COVID-19 epidemic has caused several negative effects for people, the most common of which are fever, dry cough, and weariness. A small number of people also experience nasal congestion, runny nose, and other upper respiratory and stomach problems. The majority of people on earth have contracted the new coronavirus, which is highly contagious. Additionally, some illnesses will be more serious and even fatal for the elderly or those with weakened immune systems.

Study have found that on the surface of coronavirus, there are mainly three kinds of proteins which are spike protein, envelope protein and membrane protein (figure 1). These different proteins form the hump part on the surface of virus. For spike protein, it is a key part of binding to host cells, it can

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recognize and combined with host cell surface receptors. Inside the coronavirus is nucleocapsid protein (N protein) and virus genetic information in RNA. In addition, the N protein can protect the genome of virus, and it can participate in assembly of virions or adjusting replication of the virus, eventually reach to interaction of transcription with membrane proteins. The RNA also plays an important rule in coronavirus. This is because Single-stranded RNA easily mutates as it replicates itself and the RNA of the new coronavirus has more than 30,000 bases, which is his huge reproductive base [2].

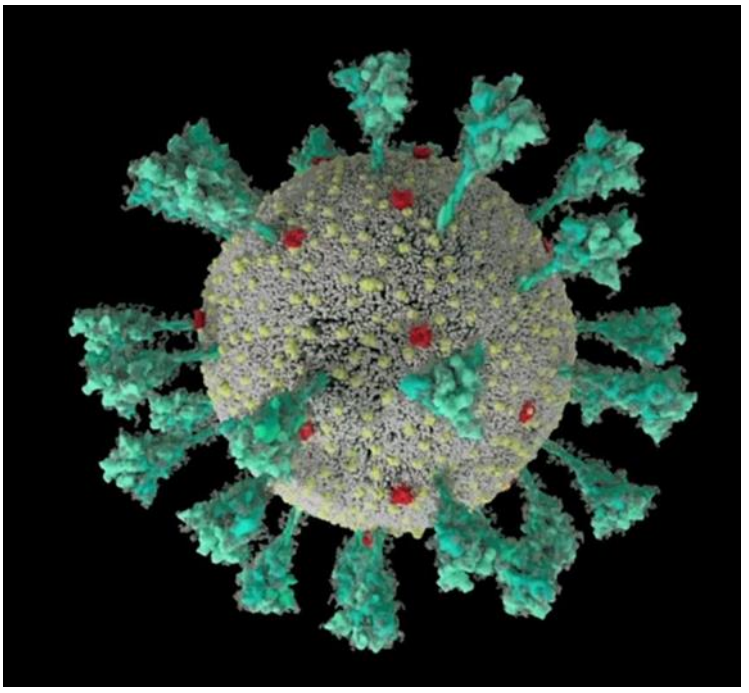

Figure 1. Modeling of the Novel Coronavirus (SARS-CoV-2)'s structure using computers. Source: Janet Iwasa, University of Utah.

There is still a lack of sufficient evidence-based medical evidence for antiviral treatment of severe COVID-19. Paxlovid/Molnupiravir is mainly targeted at patients with high-risk factors within 5 days of onset and can prevent exacerbations. For patients with severe COVID-19, only remdesivir is conditionally recommended (weakly), but this drug is currently not available in China. For critically sick COVID-19 patients, on the other hand, there are no suggested antiviral medications. Viral replication, immunological response, excessive inflammatory response, and severe illness are all pathophysiological processes that occur in severe COVID-19. The most critical period of antiviral therapy is the early stage, that is, the period of viral replication, when antiviral therapy has the best effect. Once the virus begins to replicate in large quantities and the inflammatory response appears, the effect of antiviral treatment may not be as expected [3]. This paper mainly talks about the different clinical symptoms of the three vaccines and their respective advantages and disadvantages.

2. Adenovirus vaccination

2.1. Mechanism of Preparation

Adenovirus vaccine is an adenovirus vector vaccine, which refers to the use of adenovirus as a vector to recombine the gene that can express protective antigens into the genome of adenovirus. The advantage of adenovirus vaccination is that it is especially convenient for people because only need to vaccinate once. A single adenovirus vaccination is required. For starters, people should find the adenovirus and replace spike glycoprotein, the gene for the spiny protein that is the key to the coronavirus. After virus invading in body, the virus loses its function of destroying humans, but the only function of that is to

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preserve the gene as a submit coronavirus antigen. The immune system will recognize this antigen and to produce specific immunity [4].

2.2. Clinical effect

The adenovirus vaccine is very effective, but it can give people some bad symptoms. On the basis of a work and study conducted in Wuhan, China, showed that between September 28, 29, and 30, 2020, a total of 230 people were screened for eligibility, of which 56% of the participants were 130 randomly assigned, with 26 participants in each group. One of them had an adverse reaction which was an allergic throat reaction and he was excluded from using the booster vaccine, but they were followed up and included in the final results. Each group had twenty volunteers, with 77% of them being between the ages of 18 and 55 and 23% being older than 55. In each group, 50% of the participants were men and the remaining 50% were women, and the majority of the participants and experimenters were from China.

The concentration of each group of injected adenovirus vaccines varies, and each group of doses of various vaccines is divided into various groups of experiments. Accordingly, these vaccines are divided into the following injections and vaccines: Participants in the trial received low-dose and high-dose intramuscular recombinant adenovirus vaccines, as well as high-dose and low-dose aerosol vaccines, intramuscular and aerosol vaccines (this aerosol-inhaled vaccine is painless, easy to administer, well tolerated, and strongly immunogenic).

The results showed that three groups of participants received the booster shot on day 30. Half of the 78 participants reported at least one bad episode in the week before the booster adenovirus vaccine was administered. One group had 18 cases, accounting for 69% of the total, another group had 17 cases, and the final group had 13 cases. In summary, there was no significant difference in the number of adverse reactions between each group. Also, the total number of people who still had fever within a week after the first adenovirus vaccination was 35, most of them with grade III fever. There were no serious adverse events within two months after the first vaccination of participants in either experimental group. In conclusion, the most common problems reported by the participants were fever, headache, and fatigue, and there was no cough, pain, swelling, or respiratory distress in the participants who received the aerosol versus the participants who received the other vaccine [5].

2.3. Advantages and Disadvantages

There are a lot of adverse reactions after the injection of adenovirus vaccine. According to scientific studies, there are undesirable reactions at the injection site, because the needle can damage the skin during the injection, and the adenovirus vaccine may contain some adjuvant components, which can irritate the skin and the underlying muscles, Therefore, it causes local symptoms of pain, redness, swelling and itching. The second point is that the whole body will have adverse reactions, mainly fever, headache, vomiting, diarrhea, muscle pain, fatigue and other symptoms. There are even abnormal phenomena such as difficulty breathing, loss of appetite, and fainting. Thirdly, allergy is the phenomenon. After receiving the new coronavirus vaccine, there is usually a local immune reaction and itching. This phenomenon belongs to anaphylaxis, which often manifests as redness, swelling and itching at the site of inoculation, and can resolve spontaneously in a short period of time [6]. Draw lessons from the past, people need to strengthen exercise, try to have a good immune system before vaccination, such as staying up late, drinking less, smoking less, must eat breakfast, etc., and after vaccination, we must act according to the doctor's requirements, if there are allergic phenomena or adverse reactions to report to the doctor in time. After vaccination, you need to stay for 30 minutes before you can leave, pay attention to rest, do not do strenuous exercise, light diet, to avoid adverse reactions.

3. Inactive vaccine and mRNA-based (BNT162b2, mRNA-1273) vaccines

There's another vaccine which only need two shots, and they are called inactive vaccine and mRNA-1273.The primary approach used in the study and development of inactivated viral vaccines is the cultivation of the infectious virus on the cell matrix, followed by the use of physical or chemical means to kill the infectious virus while preserving the integrity of its antigen particles, so causing it to lose

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pathogenicity but preserve antigenicity. Inactivated vaccines may contain complete viruses or bacteria or, in the case of split vaccinations, their cleaved parts.

3.1. Mechanism of Preparation

First of all, there are many different methods to make inactivated vaccines, but the most common way is chemical inactivation. Laboratory workers put live COVID-19 virus into a solution of beta-propanolactone, and other chemical agents can be used according to different properties of the virus, including ethanol and trypsin solutions with relatively high concentrations. Such a solution can make the novel coronavirus lose its original pathogenicity, use chemical reactions and mechanisms to destroy the protein structure of the pathogen, so that it cannot infect other cells and rapidly replicate itself. At the same time, it can ensure the integrity of the spiny glycoprotein. Therefore, when such a virus enters the body, it can quickly and safely cause the immune response in the human body, after that, immune cells in the body will work, such as activating T cells to engulf pathogens, and then B cells differentiation and proliferation to produce memory B cells (the process of immune response). Secondly, people are more commonly used to use physical inactivation and biological inactivation. Biological inactivation is the use of specific microorganisms, placed on the surface of pathogens, and then they will destroy the structure of pathogens. So it loses the pathogen self-reproduction and other functions, but the way of physical inactivation is more simple and rough, such as the use of ultrasound or ultraviolet light, and finally through the high temperature, but there are also need the different degree of heat of the pathogen and control the appropriate temperature, because in order to ensure the antigen is complete and cause the immune response, and finally the appropriate high temperature will reduce the pathogenicity of the virus due to the destruction of virus structures [7].

On the other hand, for mRNA-based vaccine making, the key genetic sequence of the novel coronavirus was obtained first, and this key sequence is usually the gene encoding (2.2 will explain) the spike protein on the novel coronavirus, people clone the gene sequence and insert into a plasmid vector to form a recombinant plasmid, by the way, plasmid is a genetic component made up of circular strands of DNA. It can replicate in large numbers in bacteria like E. coli, after people get such a recombinant plasmid, they can transfer it into a special type of Escherichia coli, so that this Escherichia coli can quickly replicate and mass-produce the recombinant plasmid of the gene sequence on this new coronavirus, and this process will happen after a few days, because the reproduction rate of Escherichia coli is exponential growth, and a large number can be obtained within a few days. After getting the E. coli that contains the recombinant plasmid, people dissolve the E. coli and extract the recombinant plasmid inside, and after verifying that the recombinant plasmid does not mutate, it is shown that this is the desired recombinant protein, so the staff working in the experiment cut the key sequence of the virus on the recombinant plasmid. They can cut the recombinant protein at specific sequences, and then after further separation and purification, they can get all the DNA that is the key sequence of the virus, but it is just DNA, not the mRNA people want, and the experimenters have to do the following steps to turn it into RNA. This operation requires the cooperation of many proteins and enzymes, using this DNA as a template for transcription, and it should be noted that DNA is transcribed when it exits the nuclear pore, and there are two strands on the DNA, one of which is a template strand, and the mRNA that comes out is easily mixed with the DNA template, so it needs to be purified and separated, and eventually people can have mRNA vaccines that humans want to use in vaccines [8].

3.2. Gene editing technology

The development of mRNA vaccines benefits greatly from the use of gene editing technology, a genetic engineering technique that allows for precise change of target genes or transcript products through site-directed mutagenesis, insertion, and knockout. Artificial nucleases are mostly used to remove, add, or precisely modify certain gene sequences in the genome. Because targeted genome editing can be carried out successfully, gene editing has shown tremendous application prospects in gene research, gene therapy, and genetic modification. There are now three main methods for gene editing: CRISPR-Cas9, transcription activated effector nuclease (TALEN), and zinc finger nuclease.

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3.3. Clinical effect

Different age and the number of booster needles of mRNA-1273 play big roles in this vaccine. This is because one official figure says more than 42 million people who received at least one dose of the vaccine, about 21 million received three doses of the vaccine. 5 million people were still infected with COVID-19 after vaccination, but only 3,000 people (0.007% chance of developing myocarditis) developed myocarditis within a month after vaccination or the risk of myocarditis. At the same time, the risk of myocarditis decreased gradually after the booster shot, and the same study showed that the risk of myocarditis obtained within 1 to 28 days after the first shot was 1.33 in most cases, but the rate was 1.52 or 1.57 or 1.72 after the second shot, and the rate was 5.79 or as high as 11.14 after the third shot. But one study did the same thing in people over 40, and found that people under 40 were more likely to get myocarditis than people over 40 [9]. In conclusion, mRNA vaccines can strengthen the immune system after a second or many doses. This is especially true for young adults over 40, as their improved immune function will be stronger than that of individuals under 40.

3.4. Advantages and Disadvantages

The reason why people need inoculation twice is that the addition of aluminum adjuvant and its function is to absorb and trans-antigen to recruit more B cells, dendritic cell and so on. Because of the precipitation and promotion of antigen absorption and binding, so that immune cells can strengthen the memory. So, in terms of advantages and disadvantages of inactive vaccine. The limitation of this kind of vaccine is people always need get the injection twice. People usually have to wait another six months to get a second dose of the inactivated vaccine and this is due to the weak immune response caused by the antibodies provided by the inactivated vaccine. However, compare it to the adenovirus vaccine, the immune response provided by the adenovirus vaccine is much stronger than that of the inactivated vaccine, so only one injection is needed to obtain a strong immune capacity, but its disadvantage is that compared with the weak immunity such as the elderly and children, such a vaccine may be more harmful to them, and even will not cause an immune response.

It most obvious strength is that it will not require that people with strong immunity, such as children or the elderly, can basically receive inactivated vaccines, and this vaccine is widely used in many countries, for example, most of the inactivated vaccines used in China, and that such a vaccine could survive in the body for the right amount of time without causing serious adverse effects.

4. Recombinant fusion protein COVID-19 Vaccine (V-01)

The third one is recombinant protein vaccine which three shots are required. It can take out the S protein in COVID-19, replicate it in large numbers and inject them into human bodies to induce immunity response then to generate relevant antibodies. Although there're different ways to design the vaccine, the purpose is the same. Vaccine can protect us from many diseases [10].

4.1. Clinical effect

This V-01vaccine showed good tolerance in both elderly and young adults and exhibited very good immunogenicity, which is likely to be a very promising vaccine. The recombinant protein vaccine was utilized in adults (over 18 years old) and the elderly (over 60 years old), according to pertinent study. Adults (those who were over 18) and people who were over 60 years old participated in several trials. On February 24, 2021 and after one month, about 400 people received such surveys. About half of the participants were eligible and participated in the first phase of the experiment. After grouping, young and elderly persons with average ages of 40 to 44 years old or 64 to 68 years old were separated into two groups for comparison. The first phase began one month after vaccination, with mostly male participants. Neutralizing antibody titers for live SARS-CoV-2 ranged from 64 to 113 at day 35 and from 88 to 127 at day 49, respectively. Less often than in the 18- to 59-year-old group, the 60-year-old group displayed vaccine-associated adverse events, which may indicate that reactogenicity in V-01 is missing or less severe in older individuals. Consequently, the positive safety and immunogenicity results point to V-01 as a promising option for a preventative vaccination that would benefit the majority of the older

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population. In conclusion, the novel recombinant protein COVID-19 vaccine has a very fast immune response and a strong immune response in young people, which indicates the stability of the vaccine immunity [11].

4.2. Advantages and Disadvantages

Recombinant vaccines can reduce immunogenicity, improve safety, and reduce the treatment time. The advantages of recombinant vaccines are mainly easy to store, transport, and use, and the disadvantages are mainly safety problems. But compared with inactivated vaccines, inactivated vaccines are mainly safe and easy to preserve, while the disadvantages are mainly short immunization time and large amount of vaccination. Specifically, the advantages of recombinant vaccines are mainly easy to store and transport, easy to use, simple preparation, easy mass production, and low cost. In addition, there will be the problem of immune tolerance. Gene vaccines continue to produce antigen proteins in the body, which may break the immune balance of the body and cause immune tolerance [12].

5. Conclusion

The COVID-19 outbreak has resulted in tens of thousands of deaths and severe economic losses, yet clinical interventions are limited. The emergence of a vaccine for COVID-19 is a promising solution to this problem. The first vaccine introduced in this article is adenovirus vaccine. Although such a vaccine is very effective compared with other vaccines and causes a very strong immune response, the disadvantage is obvious, it will bring bad symptoms to people. But the vaccine for the elderly is actually the V-01 recombinant protein vaccine that was also introduced, and related studies have shown that a vaccine that is more suitable for the elderly. There are still many problems that have not been solved, for example, the experimental stage of recombinant protein vaccine has only been carried out in the first and second stage, it is unknown whether the third stage is successful, whether it can be put into large-scale use, and how to strengthen the antigenicity of inactivated vaccine, or increase the working time in vivo, reduce the number of vaccination and so on. Once these problems are solved, the times of inoculation will be reduced, the pressure on any country or person will be reduced, and at the same time, it can reflect that the virus has been thoroughly resolved, and it can reduce panic and psychological pressure.

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