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COVID19 VACCINES ANALYSIS

Abstract

Objective

To deal with COVID-19, various countries have made many efforts, including the research and development of vaccines. The purpose of this manuscript was to summarize the development, application, and problems of COVID-19 vaccines.

Methods

This article reviewed the existing literature to see the development of the COVID-19 vaccine.

Results

We found that different types of vaccines had their own advantages and disadvantages. At the same time, the side effects of the vaccine, the dose of vaccination, the evaluation of the efficacy, and the application of the vaccine were all things worth studying.

Conclusion

The successful development of the COVID-19 vaccine concerns almost all countries and people in the world. We must do an excellent job of researching the immunogenicity and immune reactivity of the vaccines. We hope this review can help colleagues at home and abroad.

1 INTRODUCTION

- On December 31, 2019, a novel coronavirus disease caused by severe acute respiratory syndrome type 2 coronavirus (SARS-CoV-2) was first reported in China.[1] On January 30, 2020, the World Health Organization (WHO) announced that the new coronavirus pneumonia epidemic was listed as a "public health emergency of international concern," and on February 11, the WHO officially named the disease as Coronavirus disease 2019 (COVID-19).
- The new coronavirus is highly contagious and spreads quickly, it is not easy to find in mild cases and asymptomatic infections. Also, it is easy to cause "hidden" transmission in communities and medical institutions. The virus may gradually evolve into a seasonal low-level epidemic.
- People are looking forward to developing an effective and safe COVID-19 vaccine to contain this COVID-19 pandemic and prevent another outbreak of the epidemic. More than 200 COVID-19 vaccines have been listed in the WHO as under development. The expectations for effective prophylactic COVID-19 vaccines are very high.
- Vaccines proven effective and safe in phase III clinical trials may enter the market in 2021.
- Several vaccines have been approved for marketing, such as Pfizer-BioNTech's BNT162b2 and Moderna's mRNA-1273.

2 MAIN MECHANISM

- The design of the COVID-19 vaccines must take into account both humoral and cellular immunity.
- In addition, COVID-19 is mainly spread through the respiratory tract and contact, so the role of mucosal immunity in preventing viral infections should be paid more attention. The virus contains four structural proteins. They are Spike S protein, Envelope E protein, Membrane/matrix protein, and Nucleocapsid N protein. The S protein has two subsections, S1 and S2. The S protein binds to specific receptors, causing the virus to infect cells.
- The neutralizing antibody against the S protein can block this process and prevent the virus from invading. S protein can also effectively stimulate T-cell immune response, so it is the most important target antigen for vaccine design. N and M proteins have also been shown to induce the body to produce an efficient cellular immune response.
- The S1 subunit contains the receptor-binding domain (RBD) and is responsible for initial attachment to the host cells through the ACE2 receptor, while the S2 subunit promotes viral fusion with cells to initiate infection.
- The S protein is a frequent vaccine target as it is expected that antibodies binding to the correct epitope on the S protein may be neutralizing and block intercellular viral spread.

3 TYPES OF VACCINES

The vaccines currently under study can be roughly divided into the following categories. Different types of vaccines have their characteristics.

3.1 DNA vaccines

- DNA vaccines can enter cells like viral infections and use the host protein translation system to generate target antigens. As an endogenous immunogen, it can induce humoral and cellular immune responses at the same time.
- DNA vaccines insert genes encoding foreign antigens into plasmids containing eukaryotic expression elements and then directly introduce the plasmids into humans or animals, allowing them to express antigen proteins in host cells and induce immune responses to prevent diseases.
- The manufacturing process of plasmid DNA is relatively straightforward, and the double-strand DNA molecules are more stable than the virus and can be freeze-dried for long-term storage.
- DNA vaccine vaccination method limits its application. Since the vaccine is mainly distributed in the intercellular space after vaccination, only a very small amount can enter the cell to produce protein immunogen, so the immune effect is greatly reduced.
- A few animal DNA vaccines have been on the market, no human DNA vaccine has been approved for marketing so far. Combination with other vaccines will achieve better immune effects.

3.2 mRNA vaccines

- Compared with DNA vaccines that need to enter the nucleus, mRNA vaccines only need to enter the cytoplasm to achieve target antigens' expression, so they are theoretically safer. In recent years, mRNA vaccines have been developed rapidly.
- Many institutions at home and abroad have quickly initiated the research and development of COVID-19 mRNA vaccines.
- The mRNA vaccine developed by the National Institute of Allergy and Infectious Diseases (NIAID) and Moderna has taken the lead to initiate a phase I clinical trial. Moderna's vaccine, mRNA-1273, specifically encodes the S antigen's prefusion form, including a transmembrane anchor and an entire S1−S2 cleavage site.

3.3 Non-replicating viral vector vaccines

- One of the most explored viral vector options is the Adenovirus (Ad), currently being used by both CanSino and Oxford/ AstraZeneca.

- This gene is derived from the Wuhan-Hu-1 sequence of SARS-CoV-2 and is cloned into the E1- and E3-deleted Ad5 vector together with the tissue plasminogen activator signal peptide.
- The effectiveness of this vaccine is relatively high, but the disadvantage is that it may not effective for people with recessive infectious viruses.

3.4 Inactivated vaccines

- Inactivated vaccines are the most classic form of vaccines. They are easy to prepare and can efficiently cause humoral immune responses. They are often the first choice for new infectious diseases. Inactivated vaccines are mainly obtained through three inactivation methods, such as formaldehyde, β-propiolactone, and ultraviolet.
- Although high titers of serum neutralizing antibodies are produced, the protective effect is also not satisfied.
- Currently, the inactivated SARS-CoV-2 vaccine (Vero cells) is being used. In addition, vaccine production requires the operation of high concentrations of live viruses, which poses a certain biological safety risk.

3.5 Live attenuated vaccines

- This vaccine program has very good immunogenicity and can induce systemic immunity and mucosal immune response, and the immunity is lasting.
- Several live attenuated vaccines have been on the market, including yellow fever, smallpox, measles, polio, mumps, rubella, and chickenpox. The SARS live attenuated vaccine will recover its virulence after continuous passage in cells or mice, suggesting that the vaccine scheme has a greater biological safety risk.
- Without sufficient evidence to ensure that live attenuated vaccines will not regain strength, this strategy is not currently recommended for COVID-19 vaccine development.

3.6 Subunit vaccines

- There are currently several subunit vaccines on the market, including hepatitis B, hepatitis E, and human papillomavirus vaccines. SARS and MERS subunit vaccines can produce high-titer neutralizing antibodies in mice, and nasal or oral vaccination can also induce a mucosal immune response, thereby more effectively blocking the virus transmission through the respiratory tract. The data also prove the protective efficacy of mucosal vaccination better than intramuscular inoculation.
- It is recommended to include nasal and oral mucosal vaccination routes to activate mucosal immune responses.

3.7 Trained immunity-based vaccines

- Trained immunity-based vaccines can activate the adaptive immune system and provide pathogen-specific protection.
- Currently, Bacille Calmette-Guerin (BCG), a vaccine against tuberculosis, can induce trained immunity against COVID-19 and is currently undergoing clinical evaluation, which will take time to prove,

4 QUESTIONS AND THOUGHTS

There are always various problems in the development of vaccines. Among them, the later application and evaluation of vaccines are particularly prominent.

4.1 Dosage problems

- In this case, another special dosage consideration is age. The immune function that declines with age may lead to a greater risk of severe COVID-19 in the elderly and lead to low vaccine responses.
- As observed in the influenza vaccine, is a large dose of the COVID-19 vaccine needed to protect the elderly effectively? It may take some time to solve these problems.

4.2 Adverse reactions of vaccines

- The vaccine also has adverse reactions such as redness, swelling, muscle pain, and fever.
- The preferred requirements for effectiveness include the protection effectiveness in the population is at least 70%, and the same is true for the elderly. If it is an outbreak treatment, the protective effect must appear within two weeks and last for at least one year.
- The most basic requirements include the population's protective effect is at least about 50% for at least six months.

4.3 Clinical trials and Efficacy evaluation (endpoint observation)

- Key considerations for the safety of COVID-19 vaccine research and development were important.
- Therefore, when studying COVID-19 vaccines, attention should be paid to whether they will cause similar immunopathological reactions. Long-term safety observations are required.

4.4 Vaccine application

- Preventive vaccines will control COVID-19 is justified by the impact of vaccines on preventing disability and death from infectious diseases.
- Therefore, vaccination is particularly important in global epidemic prevention work.

4.5 Travel immunization

If the epidemic situation is well controlled, and the future epidemic situation is mainly imported, entry and exit personnel should be the target of implementing the immunization strategy, and close contacts of entry personnel should be used as vaccinations.

4.6 Immunization after exposure

If it is confirmed that the COVID-19 vaccine has the effect of preventing or alleviating the symptoms of the disease on the exposed subjects, it is possible to consider adopting a post-exposure immunization strategy for close contacts of confirmed COVID-19 cases.

4.7 Pre-exposure immunization

For subjects who may be exposed to COVID-19 patients or high-risk infections, such as medical staff in fever clinics, COVID-19 pathogen testing personnel, contact persons from COVID-19 endemic countries, etc., should take exposure pre-immune prevention strategies.

4.8 Emergency immunization

In the event of a COVID-19 epidemic, under the premise of confirming the emergency immunization effect of the COVID-19 vaccine, an emergency immunization strategy can be considered for the population in the epidemic area.

In the case of vaccine supply in batches, comprehensive consideration of protection priorities, reducing deaths and cluster outbreaks determine the targets and immunization procedures for mass pandemic vaccination.

5 CONCLUSION

In short, the successful development of the COVID-19 vaccine concerns almost all countries and people in the world. We must do an excellent job of researching the immunogenicity and immune reactivity of the vaccines.