Editorial Communication

Fighting Approaches Against COVID-19: For Now and the Future

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ABSTRACT

In the past 3 years, from 2019 to the present, the world has experienced a life-threatening COVID-19, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It has caused more than 6 million deaths and this number continuously increases. Drugs and vaccines are the top 2 approaches to fight COVID-19. Some drugs were developed as antiviral drugs, while others were not primarily synthesized as antiviral drugs but have been used and claimed to be effective for COVID-19 treatment. However, drug can be used only therapeutically but not prophylactically. Vaccines have become appropriate choices for preventing people from COVID-19 infection; hence, reducing infection and death cases caused by SARS-CoV-2. Currently, COVID-19 vaccines have been developed by several approaches. Due to the high mutation rate of COVID-19 virus, drugs and vaccines against COVID-19 have to be continuously developed to protect people from the disease This communication discusses some of the fighting approaches against Corona Virus Disease 19.

KEY WORDS: COVID-19, SARS-COV-2, ANTIVIRAL DRUGS, VACCINES.

From 2019 up to the present day, the world has experienced a pandemic of COVID-19, a life-threatening disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The disease originating in Wuhan, China has spread across more than 200 countries around the world resulting in enormous health, lives, and economic losses. It has changed the way people live and work fundamentally. The SARS-CoV-2 is closely related to SARS-CoV (severe acute respiratory syndrome coronavirus) which spread in a global pandemic in 2003 and MERS (Middle East respiratory syndrome coronavirus) which caused an outbreak mostly in the Middle East in 2012. Symptoms of COVID-19 are milder than SARS and MERS, but it transmits from human-to-human faster than they do, causing more infected cases. However, the mortality rate of COVID-19 is lower (less than 2%) than that of SARS (10%) and MERS (35%) (House et al. 2021). Up until January 2022, cumulative number of infected cases and deaths worldwide is more than 330 million and 5 million, respectively.

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If we asked the general public what are appropriate approaches, based on what we have and what we can do now, to fight COVID-19. The top 2 answers given the most would be antiviral drugs and vaccines. Are these approaches exactly appropriate for now and the future? Antiviral drugs are drug administrated mainly for inhibiting viral replication inside host cells. Most of them are nucleoside analogues resemble naturally occurring nucleosides and act by inhibiting the synthesis of viral nucleic acids. Antiviral drugs that have been used for treatment of COVID-19 are drugs previously developed to treat other viral infections such as ribavirin (a drug for hepatitis C virus), ritonavir (a drug for HIV virus) and favipiravir (a drug for influenza virus) (Gil Martinez et al. 2021).

Some drugs were not primarily synthesized as antiviral drugs but have been used and claimed to be effective for COVID-19 treatment. For examples, hydroxychloroquine and chloroquine primarily used to treat malaria have been shown to kill the COVID-19 virus in vitro. They were found to prevent the virus to attach to the cell, inhibiting the virus from entering the cell and multiplying within it (Tripathy et al. 2020). Although no specific antiviral drug has been proven effective for treatment of patients with

COVID-19, one drug that has received a lot of attention is the antiviral drug remdesivir (Eastman et al. 2020). It is an adenosine analogue prodrug that has a broad antiviral spectrum against many viruses including filoviruses, paramyxoviruses, pneumoviruses, and coronaviruses. The drug was intentionally developed to treat RNA viruses that maintained global pandemic potential such as those causing EBOLA, SARS and MERS. Remdesivir is the first treatment for COVID-19 to be approved by the U.S. Food and Drug Administration (FDA) in October 2020.

However, the effectiveness of the drug is still in question. Furthermore, in November 2020, the World Health Organization (WHO) has issued a conditional recommendation against the use of remdesivir in hospitalized patients, regardless of disease severity, as there is currently no evidence that remdesivir improves survival and other outcomes in these patients.

Antiviral drugs, we have had so far, might not be appropriate for the future as a fighting approach against COVID-19 because they can be used only therapeutically with low effective rates but not prophylactically. Moreover, the high mutation rate of COVID-19 virus makes the drugs less effective. However, they are still required for now, at least to somewhat reduce the number of hospitalized patients and deaths.

Vaccines are biological products that produce immunity to a specific pathogen (either bacteria or virus). When the body receives a vaccine, it stimulates the body's immune system to be ready to fight a specific pathogen that the body has not come into contact with before. Here, the focus is on just vaccines for viral diseases. Vaccines can be classified into 3 groups, first, second and third generation vaccines, based on their development technologies (Tahamtan et al. 2017).

The first generation vaccines include live attenuated vaccines and inactivated vaccines. This group of vaccines is produced by using the oldest technology as the production of the very first vaccines in the 19th century. Whole viral particles are produced in living organisms such as chicken embryos, then attenuated or killed (inactivated) and used as live attenuated vaccines and inactivated vaccines. These vaccines have high ability to stimulate innate immunity but in the same time have high risk of causing disease due to the use of complete pathogen.

The second generation vaccines are produced by using recombinant DNA technology. To produce these vaccines, genes encoding the immunogenic proteins of pathogens have to be identified and genetically engineered. They can be produced in the forms of immunostimulatory protein subunits or viral vector based vaccines by using modified viruses (the vectors) to deliver recombinant DNA into recipients. By doing this, they have less risk of causing disease compared to the first generation vaccines. However, the process of identifying the immunogenic subunits or proteins of pathogens is time consuming and requires sophisticated technology.

For the third generation vaccines, RNA encoding immunogenic proteins are used as vaccines. These vaccines use the recipients' bodies as manufacturers to produce immunogenic proteins instead of producing them in a large quantity in laboratories as the first and second generation vaccines. Therefore, they can be produced with less time and cost compared to the first and second generation vaccines. However, RNA vaccines have difficulty in storage and transport due to their tendency to be degraded easily.

In general, the production of a vaccine includes 3 steps:
As drug production, the production and evaluation of vaccines includes 3 steps: identify and producing antigens or immunogens, tests on animal models (preclinical trials), and clinical trials. To test for safety and efficacy, every vaccine has to go through three phases of clinical trials. After the vaccine passes all three trial phases, it can be submitted to the WHO and various government agencies for approval. The whole process takes time ranging from 5 to 15 years, (Tahamtan et al 2017).

Vaccines available todays were produced following this timeline. However, the normal vaccine development timeline is not good enough for COVID-19 pandemic having more people infected and died every day. The shortened timeline for COVID-19 vaccine development will make a huge difference to the world in terms of saving lives and reducing trillions of dollars in economic damage.

Many strategies are applied to compress the timeline to as little as 18 months. For example, manufacturers start to produce different potential vaccines at the same time as the clinical trials are still going on. Furthermore, FDA has issued an Emergency Use Authorization (EUA) to enable emergency use of potential vaccines before approval.

The most promising COVID-19 vaccine candidates are developed by variety of approaches. Several of them have been approved for emergency use. CoronaVac, also known as Sinovac vaccine, and BBIBP-CorV, also known as Sinopharm vaccine, are examples of the vaccines developed by the first generation vaccine technology while Gam-COVID-Vac, also known as Sputnik V vaccine, and AstraZeneca vaccine are viral vector based vaccines produced by the second generation vaccine technology. The popular RNA based vaccines are Tozinameran, also known as Pfizer-BioNTech vaccine, and Moderna vaccine.

Even if these candidates and others are proven to be promising, developing the vaccine is just the first step. Although COVID-19 vaccines available todays may not be

the perfect ones and still be in the developing and approval process, there is a light at the end of the tunnel. Sooner or later a COVID-19 vaccine that is approved and licensed will become available. It will bring the world back to the way things were before the COVID-19 pandemic.

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