DOI: 10.4274/csmedj.galenos.2022.2022-11-5
Cam and Sakura Med J 2023;3(3):86-90
CSMJ

COVID-19 Vaccines

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ABSTRACT

The novel coronavirus is an infectious disease caused by severe acute respiratory syndrome coronavirus-2. The World Health Organization declared coronavirus disease-2019 (COVID-19) outbreak is a pandemic in 2020. Many people die of acute respiratory failure both in community and hospital. Therefore, there is an urgent need for a novel effective treatment or vaccine to combat the outbreak. To develop new vaccine, a wide variety of studies have been conducted in many countries. Some vaccines are approved by the Food and Drug Administration. They were developed by a variety of techniques; mRNA, inactivated, recombinant and vector-based vaccines. Most of them are safe and effective, but some adverse reactions have been observed. COVID-19 vaccination prevented spread of the virus and halted the outbreak, by breaking the chain of the infection. Thus, the pandemic has proven again that vaccination is essential for human health. In this article, we attempted to review the commonly used ones in clinical practice.

Keywords: Coronavirus, COVID-19, pandemic, vaccines

CAM & SAKURA MEDICAL JOURNAL

Introduction

The coronavirus disease-2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). The disease first appeared in China and the virus infected many people, leading to various diseases from asymptomatic to severe infection. Then it spread worldwide and the World Health Organization declared COVID-19 as a pandemic on March 11, 2020 (1). During the disease, many people developed severe pneumonia and died of the infection in the community and in the hospital due to acute respiratory failure. Therefore, there is an urgent need for a novel treatment or vaccine to combat the outbreak. To develop new vaccine, a wide variety of studies have been conducted in many countries. Some of them were approved by the Food and Drug Administration (FDA) and administered to humans with immense effort. They developed various techniques (2). They were mRNA, inactivated, recombinant and vector-based vaccines.

1. mRNA Vaccines

mRNA technology has been used for more than 20 years and displays promising potential for developing new vaccines against various diseases, including cancer and infections (3). mRNA vaccines for SARS-CoV-2 absolutely represent a novel vaccine approach. It works very differently from conventional vaccines. Conventional methods allow the body to produce antibodies by administering an antigen or a viral vector that encodes an attenuated virus or synthetic antigen (4). As their contents are prepared and generated outside the human body, it needs lots of time. Such vaccines are injected into the human body, but do not enter the human cell. However, mRNA vaccines contain

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Received: 07.11.2022 **Accepted:** 09.11.2022

synthetic mRNA molecules that encode vaccine antigens within nanoparticles (5). The mRNA sequence of the virus was directly inserted into a human cell, thereby re-programing the human cell to produce its own viral antigens. The adaptive immune system then activates, newly develops antibodies bind to the antigen and T-cells are activated. Additionally, the use of mRNA has several beneficial features compared with previous vaccines. As mRNA-based vaccine is non-infectious, there is no potential risk of infection and the other benefits are rapid, inexpensive and manufacturing (3).

There are two mRNA vaccines including BNT162b2 (Pfizer-BioNTech COVID-19 vaccine) and mRNA-1273 (Moderna COVID-19 vaccine). Both are monovalent vaccines. The latter is approved by the FDA for individuals aged 12 years and older and for children 6 months to 11 years of age, it is available under emergency use authorization (EUA) (6). Two doses of 30 mcg are administered intramuscularly a three to eight-week interval. For immune-compromised host, a third dose is given at least 28 days after the second vaccination (7). The former is approved by the FDA for persons aged 18 years and older and is available under EUA for children 6 months to 17 years of age (8). For certain immune compromising conditions, the recommendations are the same as Pfizer-BioNTech vaccine.

In some observational and surveillance studies, both vaccines have been considered safe (9,10,11). In the phase 3 clinical trials of both vaccines, some local and systemic adverse reactions were observed. An analysis showed that both mRNA vaccines were related to the risk of myocarditis and pericarditis in people aged 18-39 years (about 22.4 and 31.2 cases per million doses, respectively) (12). Safety studies stress that the risk of myocarditis following infection is much higher than after vaccination (13). In a post-authorization study, acute allergic reactions were also seen as a potential outcome (14). In a study reviewing adverse events among healthcare workers, 98% of them had no symptoms of an allergic reaction. Compared to Pfizer-BioNTech, acute allergic reactions were mildly more frequent with the Moderna vaccine. Anaphylaxis was observed at a rate of 2.47 cases per 100.000 vaccination and the rate was similar between the two vaccines (11,15). Existing observational studies demonstrated that most reactions reported by children after receiving Pfizer-BioNTech were mild in severity. It most frequently occurs the day after vaccination and is transient (16). However, an analysis reported higher rates of myocarditis following the second dose of mRNA vaccinations among adolescent men and young adults (17). Following COVID-19 infection, these results are still much rarer among pediatric and adolescent populations (18).

The efficacy of both vaccines with two doses in preventing symptomatic COVID-19 infection in persons without previous COVID-19 has been found to be high (19,20). mRNA vaccination (>14 days after second dose) prevented hospitalization in 89%, intensive care unit admission in 90% and admission to emergency unit in 91% of the cases (21). The efficacy rate was similar to Pfizer and Moderna vaccines in these three categories and ranged from 81% to 95% in people older than 50 years (22). Among all adults, a study from Israel reported that its effectiveness for preventing death from COVID-19 was approximately 72% (23). Another study reported in early 2020 found that both mRNA COVID-19 vaccines were approximately 90% effective in preventing both symptomatic and asymptomatic infections (24). Studies conducted in the United States of America (USA) revealed that the effectiveness of the Moderna and Pfizer vaccines in preventing hospitalization was 93% and 88%, respectively (25). In another USA study evaluating BioNTech, the effectiveness in preventing infection and hospitalization was 73% and 90%, respectively. Efficiency of full vaccination against infections decreased from 88% in the first month to 47% in 5th month (26).

2. Viral Vector Vaccines

Viral vector vaccines use the viruses to transfer genes encoding vaccine antigens into body cells. Adenoviruses are the most commonly used viruses as a viral vector. The vaccine transfers the virus, which will circulate in the nucleus. The genes are expressed in the nucleus by developing the antigen, and then the induction of an immune response is commences (27). The vectors can be replicating or non-replicating. There are three viral vector vaccines, including the Johnson & Johnson/Janssen, the Oxford-AstraZeneca and Sputnik V COVID-19 vaccines.

All these vaccines are considered highly effective and appear to wane over time to mRNA vaccines. All of these are safe but rare blood clotting was observed in the first 2 vaccines (28). Another study reported an increased incidence of Guillain-Barré syndrome following vaccination with the first vaccine (29). The efficacy of the Janssen vaccine was 68% against COVID-19 infection and against COVID-19-related hospitalization was 71% in all adults (22,25). After a single dose given, the AstraZeneca vaccine demonstrated significant efficacy of 64.1% against symptomatic COVID-19 and 70.4% after two doses and the phase 3 study showed vaccine efficacy of 76% against symptomatic COVID-19 infection and 100% efficacy in preventing severe disease (30). In people receiving Sputnik V, the phase 3 results have showed 91.6% effectiveness after the first dose of vaccine and 100% effective in preventing severe COVID-19 disease (31,32).

3. Recombinant Vaccines

Protein subunits (only a selected antigenic part of virus) or virus-like particles are used for this method. Most sort of these vaccines focus on the virus's spike protein or its receptor binding domain. NVX-CoV2373 (Novavax, USA) was developed using this technology. It contains 5 µg of a recombinant full-length spike trimer as the main antigenic component and 50 µg matrix M1 adjuvant (33,34). Primary vaccination series includes two doses of vaccine with 21 days interval. The vaccine has EUA for individuals 12 years and older (33). In the phase 3 trial of Novavax, infection rates were 0.01% and 0.8% in the per-protocol group (people vaccinated with 2 doses) and placebo groups, respectively (35). All COVID-19 cases had mild infection and the vaccine was found to be 100% effective against moderate to severe infection. Most common solicited adverse events are injection site tenderness/pain, headache, myalgia, fatigue, and malaise within two days (35). In another clinical trial, ten of 7020 individuals in the per-protocol population (7 days after 2 dose vaccination with NVX-CoV2373) infected with SARS-CoV-2. None of them were hospitalized or died of COVID-19. One patient developed vaccination-related myocarditis and no anaphylaxis was observed (36).

In different studies, both local and systemic adverse reactions were seen more commonly in the vaccinated group and frequent complaints were injection site pain/tenderness, erythema, swelling, headache, muscle pain, fatigue, nausea, and vomiting. The adverse events usually were not severe (34,35,36).

4. Live Vaccines

Live vaccines use an attenuated form of the germ that leads to a disease. Since they contain all virus components, they induce both humoral and cell-mediated immunity, thereby developing a strong and long-lasting immune response.

5. Inactivated Vaccines

Inactivated vaccines are a type of conventional vaccine produced by whole virus or bacteria. A large quantity of live viruses and biosafety level-3 laboratories are required. SARS-CoV-2 viruses are inoculated into African green monkey kidney cells (Vero cell) for multiplication of virus. After yielding much viruses in culture, they are inactivated by some chemicals (37,38). All these steps take a lot of time. CoronaVac/Sinovac and Turkovac are inactivated COVID-19 vaccines. Because the vaccines contain whole virus components, immune responses can develop against viral antigens including nucleoprotein, envelope, matrix, and spike protein, thereby evoking both cellular, and humoral immunity (19). However, antibodies decrease over time, resulting in the need for booster doses (39).

Sinovac is the most widely used inactivated vaccine, developed in China. It includes an alimunium hydroxide adjuvant and is intramuscularly administered with 2 doses an interval of 2 to 4 weeks. It is also available in some other countries including Brazil, Chile, Indonesia, Mexico, and Turkey. In a phase 3 study in our country, the effectiveness of this vaccine was 83.5% (40). However, some trials from different countries reported lower efficacy (41,42). In Chile, the vaccine effectiveness was approximately 70% against SARS-CoV-2 infection and 86%-88% in preventing COVID 19-related hospitalization and death (43). A study in Brazil showed lower efficacy (47%) in the elderly (>70 years) for preventing COVID-19 infection. Its efficacy was also reported 56% and 61% for preventing hospitalization and mortal outcome, respectively (44).

Generally, this vaccine is considered as safe, but some mild and moderate adverse reactions have been observed. Injection site pain was one of the most reported reactions and fatigue was the main compliant (41,45,46,47).

ERUCoV-VAC/TURKOVAC is also inactivated vaccine developed with the support of the Health Institutes of Turkey. Vero E6 cells are used for the vaccine production. It is administered intramuscularly twice with 28 days apart. In phase 2 studies, the vaccine was evaluated on three animal models; BALB/c mice, K18-hACE2 (transgenic mice), and ferret. BALB/c mice and ferret models showed to be safety profile of the vaccine. BALB/c mice model demonstrated that the vaccine induced enhanced immunogenic response. Recently, ferret models suggested the vaccine reduces the number of upper respiratory tract infections and protects from lethal disease. The vaccine was authorized by the Turkish Medicines and Medical Devices Agency in December 2021. The phase 3 clinical trials are still in progress since June 2021.

Vaccination practice in Turkey: SARS-CoV-2 vaccination began in Turkey on January 14, 2021. The vaccines currently used are the BioNTech, Sinovac and Turkovac vaccines. A total of 151,999,998 doses of vaccine were administered in Turkey. The number of people who received 3 doses of vaccine was 28,214,781 (48). There are 3 clinical (1 phase1, 1 phase2, 1 phase3) and 6 preclinical vaccine studies are still in progress in Turkey (49).

Conclusion

Studies across the world indicated that COVID-19 vaccines are safe and effective. It is also crystal clear that vaccination

prevents the spread of the virus and halt COVID-19 outbreak, by breaking the chain of the infection. Their benefits outweigh some vaccine-related adverse reactions. Vaccines are crucial for human health and this has been proven once again by their role in controlling the pandemic.

Ethics

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: S.Y.K., A.K., B.M., Design: S.Y.K., A.K., B.M., Data Collection or Processing: S.Y.K., A.K., Analysis or Interpretation: S.Y.K., A.K., B.M., Literature Search: S.Y.K., A.K., Writing: S.Y.K., A.K., B.M.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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