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Efficacy of the Vaccines, Their Safety, and Immune Responses against SARS-CoV-2 Infections

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Abstract The search for vaccines has been a high priority since the worldwide COVID-19 pandemic was declared. Currently, mRNA-based vaccines, adenovirus-based vaccines, inactivated virus vaccines, and other vaccine platforms are all employed to combat the SARS-CoV-2 virus. BNT162b2 and mRNA-1273 are mRNA-based vaccines. The vaccination appears to be effective against SARS-CoV-2 strains that have emerged since the first study. They have primarily minor side effects, and there are no major safety concerns. Adenovirus-based vaccines are delivered by genetic cargo that is based on non-replicating adenovirus vectors that can increase immune response without the need of adjuvants. This is the case for Ad26.CoV2.S, ChAdOx1 nCoV-19/AZD1222, Gam-COVID-Vac/Sputnik V andAd5-based COVID-19 vaccine. There have been no known incidences of allergy to adenovirus vaccines, unlike mRNA vaccines. Inactivated virus vaccines are a common form of vaccine that has been used for decades. The goal is to render the virus non-infectious while preserving immunogenicity with high-quality antigens in order to trigger an immune response. The researched formaldehyde-inactivated whole-virus SARS-CoV2 vaccine (CoronaVac), as well as WIV04 and HB02, utilize this sort of vaccine formulation. A recombinant protein nanoparticle vaccine named NVX-CoV2373 is made up of trimeric spike glycoproteins with a potent Matrix-M1 adjuvant. Against the variant B.1.1.7 (Alpha), the vaccine appeared to be very effective. Vaccine efficacy against the B.1.351 (Beta) strain, on the other hand, proved to be lower.

Keywords: *COVID-19, efficacy, immune response, safety, vaccines*

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1. Introduction

Corona virus disease 2019 (COVID-19) is caused by the severe acute respiratory syndrome corona virus-2 (SARS- CoV-2) [1,2]. SARS-CoV-2 has not been fully controlled yet, and coronavirus disease pandemic of 2019 (COVID-19) continues to pose a threat to global public health [3,4]. Many interventions, such as mask use, quarantining, and social distance, have helped to prevent the spread of COVID-19, but vaccination is the most effective strategy to stop the pandemic from spreading [5]. Its success is contingent on the creation of safe and effective vaccines as well as public acceptance [6].

Clinically available COVID-19 vaccines have been developed at an extraordinary rate in the last year. According to WHO's most recent data, at least ten different COVID-19 vaccines based on multiple technologies have been approved for emergency clinical use or conditional marketing [4]. Vaccines given intramuscularly or intradermal elicit mostly IgG and no secretory IgA [7]. Most vaccines currently in development may potentially induce disease-preventing or disease-attenuating immunity, but not necessarily sterilizing immunity [8].

Vaccine development can be divided into three categories as traditional approaches to vaccine development (inactivated or live-virus vaccines), platforms that have recently resulted in licensed vaccines (recombinant protein vaccines and vectored vaccines), and platforms that have yet to result in a licensed vaccine (RNA and DNA vaccines) [8]. One of the most significant requirements for COVID-19 vaccines for mass immunization is to demonstrate their safety through clinical data [9]. As a result, the aim of this paper is to review efficacy of the vaccines, their safety, and immune responses against SARS-CoV-2 infections.

2. mRNA Based Vaccines

Vaccines based on attenuated mRNA viruses, such as Mumps, Measles, and Rubella, immunize by transferring their mRNAs into the cells of the vaccinated individual, who subsequently produce viral proteins that trigger the immune response [10]. The mRNA molecule is

meticulously adjusted to avoid unwanted reaction and given via lipid nanoparticle systems to ensure successful delivery, which has considerably aided the success of SARS-CoV-2 vaccines. The first mRNA vaccinations in healthy people were BNT162b2 (Pfizer-BioNTech COVID-19 vaccine) and mRNA-1273 (Moderna COVID-19 vaccine) [11].

Immune response: Dendritic cells, acting as antigen-presenting cells (APCs), take up the mRNA after an intradermal injection and transport it to the lymph nodes. By delivering mRNA molecules to T-cells and stimulating their proliferation and activation, the APCs initiate adaptive immunity [12]. Particularly, mRNA vaccines are effective because they can induce both humoral and cellular adaptive responses, activating T-cell helper and cytolytic T-lymphocytes [13].

Efficacy of the vaccines: A single mRNA vaccination dosage appears to be adequate to achieve protection in SARS-CoV-2 naturally infected individuals [1]. In clinical trials, BNT162b2 and mRNA-1273 showed more than 90% efficacy against SARS-CoV-2 clinical infection. This high vaccine efficacy is accompanied by a low number of side effects [14]. BNT162b2 was proven to be safe and efficacious against COVID-19 in a two-dose regimen (30 g per dosage, given 21 days apart) [15]. Observational data from several countries following national BNT162b2 roll-outs back up the trial results [16]. It is mentioned that mRNA-1273 demonstrated 94.1 percent vaccine efficacy in preventing symptomatic COVID-19 at or after 14 days following the second dose in a major placebo-controlled phase III study [17]. Observational evidence on vaccine effectiveness backs up the trial results [18,19].

Safety of the vaccine: The vaccine BNT162b2 has a good safety profile [20], however, it has a lot of minor side effects (injection site pain, weariness, headache, chills, muscle soreness, and joint pain) [21]. In mRNA-1273, half of the participants had side effects from the vaccine, including fatigue, chills, headache, myalgia, and discomfort at the injection site. However, there were no major safety concerns raised [10].

3. Adenovirus-Based Vaccines

Because of their potential to generate both innate and adaptive immune responses, adenoviruses are regarded excellent vectors for delivering target antigens to the mammalian hosts. They have the ability to stimulate immunological response without the need of adjuvants [22]. This is the case with Ad26.CoV2.S (Janssen/Johnson and Johnson COVID-19 vaccine), which is based on a replication-incompetent adenovirus 26 vector that expresses a stabilized spike protein, ChAdOx1 nCoV-19/AZD1222 (University of Oxford, AstraZeneca, and the Serum Institute of India), which is based on a replication-incompetent chimpanzee adenovirus vector that expresses the spike protein, Gam-COVID-Vac/Sputnik V (Gamaleya Institute) uses two replication-incompetent adenovirus vectors to express a full-length spike glycoprotein, while Ad5-based COVID-19 (Can Sino Biologics) uses a replication-incompetent adenovirus 5 vector to express the spike protein [23,24].

Immune response of the vaccines: Through the expression of transgenic products, this form of vector stimulates effective immune responses and mimics the true infection. The introduction of (non-replicating) viral vectors allows not just antibody expansion but also a robust cytotoxic T response with the ability to destroy infected cells to be signaled [25]. Epitopes expressed in the capsid and presented by APCs via MHC class I and II are included in the vector's design. Because most adults have been infected with many adenoviruses, memory T-cells are induced, and anti-adenovirus effector memory cells are reactivated as a result [8].

Efficacy of the vaccines: Ad26.CoV2S demonstrated 66.9% efficacy in preventing moderate to severe/critical COVID-19 (which comprised patients with pneumonia, dyspnea, tachypnea, or at least two symptoms of COVID-19) starting at or after 14 days following vaccination in a phase III efficacy trial [26]. Overall efficacy was reported to be 74 percent in the United States, 66 percent in Brazil, where the Gamma (P.2) variety was common, and 52 percent in South Africa, where the Beta form caused the majority of infections (B.1.351). The vaccine efficacy of ChAdOx1 nCoV-19/AZD1222 is higher when participants receive a low-dose followed by a standard dosage 90 percent of the time, compared to two standard-dose recipients 62.1 percent of the time [27]. In a press release announcing the preliminary results of a placebo-controlled trial undertaken in the United States, Chile, and Peru, identical outcomes were reported [28]. Data from effectiveness trials for the Ad5-based COVID-19 vaccine have yet to be published; a phase 3 trial is now underway worldwide and is expected to be finished by January 2022 [29]. According to a phase III research, Gam-COVID-Vac/Sputnik V had a protective efficacy of 91.6 percent against COVID-19 infection [30].

Safety of the vaccines: The adverse effects of Ad26.COV2.S vaccine is nausea, discomfort, and swelling at the injection site, fatigue, myalgia, and ChAdOx1 nCoV-19/AZD1222 vaccination side effects include nausea, pain, warm sensation, and tenderness at the injection site, chills, exhaustion, headache, and malaise [12]. There have been no known incidences of allergy to adenovirus vaccines, unlike mRNA vaccines [16]. Long-term consequences are still being studied, but allergic reactions are a common side effect of vaccination, and there is no reason why the vaccinations should not be given to those who have never had an allergic reaction [4].

4. Inactivated Virus Vaccines

The inactivated viral vaccine is a common form of vaccine that has been used for decades. The goal is to render the virus non-infectious while preserving immunogenicity with high-quality antigens in order to trigger an immune response [22]. This type of vaccine formulation is used for the investigated formaldehyde-inactivated whole-virus SARS-CoV2 vaccine (CoronaVac) and WIV04 and HB02 (Sinopharm) are inactivated, whole-virus vaccines based on two separate SARS-CoV-2 isolates from patients in China; they each feature an aluminum hydroxide adjuvant [31,32,33].

Immune response of the vaccines: The mechanism is that vaccines results in monocyte activation boosts IFN expression, which activates CD4+ T cells, enhancing antibody release by B cells, as well as CD8+ cells, facilitating the death of infected cells [34]. With a second injection, Corona Vac evoked 92.4 percent seroconversion in subjects after two weeks and 97.4 percent after four weeks [35]. Six weeks following immunization, a high titer of antibodies was also found [36].

Efficacy of the vaccines: In a phase III efficacy trial involving approximately 40,000 people without a prior evidence of SARS-CoV-2 infection, vaccine efficacy was assessed to be 73 percent for WIV04 and 78 percent for HB02 14 days after full vaccination, when compared to an alum-only placebo [37]. CoronaVac has a good efficacy and safety profile in a population aged 18–59 years old against symptomatic SARS-CoV-2 infection and severe COVID-19 infection [38]. CoronaVac had a 50.7% overall efficacy against symptomatic COVID-19 14 days or more after the second dose; however, the efficacy against moderate and severe cases was 100% [39].

Safety of the vaccines: Patients in phase I and II trials had a low percentage of adverse events and demonstrated immunogenicity. CoronaVac was provided to individuals aged 60 and older in phase III trials and 20 percent of participants experienced adverse effects, including injection site pain and mild-to-moderate symptoms. A small percentage of major adverse effects (2%) were determined to be unrelated to vaccination [40]. Injection site pain and fever were the most prevalent adverse effects to WIV04 and HB02, both of which were minor and self-limiting [41].

5. Other Vaccine Platforms

The recombinant protein nanoparticle vaccine NVX-CoV2373 (Novavax) is made up of trimeric spike glycoproteins with a potent Matrix-M1 adjuvant [42]. NVX-CoV2373 exhibited 90.4 percent efficacy in preventing symptomatic COVID-19 commencing at or after seven days following the second dosage in seronegative patients, according to a press release about a phase III efficacy trial in the United States and Mexico [43]. Adult subjects received a two-dose NVX-CoV2373 vaccination, which provided 89.7% protection against SARS-CoV-2 infection and demonstrated high efficacy against the B.1.1.7 variant [44]. However, vaccine efficacy was lower in a smaller experiment in South Africa, where the B.1.351 (Beta) form produced the majority of COVID-19 cases, at 49.4 percent. Reactogenicity events were more common, which included tenderness or pain at injection site, fatigue, and muscle pain [45].

6. Conclusion

Vaccination is a critical component of the SARS-CoV-2 pandemic, as it prevents new infections and saves millions of lives. Meanwhile, new vaccines are being evaluated in preclinical and clinical trials and a range of technologies are helping to develop novel vaccination strategies. The introduction of novel COVID-19 strains is also a major worry that should be taken into account for current and future vaccines. Further research on immunization schedules, such as more frequent vaccines or a larger dose per injection, or nasal vaccine is required.

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Contribution of Authors

All the authors contributed equally. They read the final version, and approved it for the publication.

Conflict of Interest

The authors declare that they do not have conflict of interest.

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