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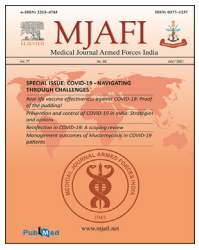

Perspective

Coronavirus disease 2019 vaccines: perspectives and update

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Introduction

The history of vaccination (which aims to reduce infectious diseases and combat epidemics) dates back to almost three hundred years.[1] The eradication of smallpox from the world in 1980 was a success story of the vaccination in combating deadly diseases with epidemic potential. Since December 2019, the world is suffering from coronavirus disease 2019 (COVID-19) pandemic, with more than 176 million cases and 3.8 million deaths.[2] A comprehensive vaccination program against COVID-19 can play a pivotal role in protecting people from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection efficiently and sustainably, resulting in complete elimination or significantly reduced transmission within the herd population. High vaccination coverage provides herd immunity for unvaccinated population.[3] The COVID-19 pandemic has seriously affected the livelihood of the community and the morbidity and mortality of the population. Still, efficient vaccination strategies can significantly improve life expectancy, thus fundamentally reshaping society and the economy.

The genetic sequence of SARS-CoV-2 was made available within weeks after its discovery and was identified as a beta coronavirus with close genetic similarity to severe acute respiratory syndrome coronavirus.[4,5] Through public and private sector involvement, many countries started the arduous task of developing a safe and effective vaccine within record-breaking time. The World Health Organization (WHO) launched Access to COVID-19 Tools Accelerator by the end of April 2020, promoting innovation and collaboration in four pillars of work: diagnostics, treatments, vaccines, and health system to strengthen the response for COVID-19 by bringing various stakeholders on board.[6] World economies involved in developing vaccines faced multiple challenges from choosing the category of vaccine, design, manufacturing system to cold chain requirements and local and global distribution strategy.[7]

According to the WHO landscape documents, there are 182 vaccines in the preclinical and 74 in clinical stages as of 18 February 2021. Vaccine candidates for COVID-19 fall into one of ten groups which include live attenuated, inactivated, protein subunit, virus-like particles, virus vectored (non-replicating and replicating: with or without antigen-presenting cell), mRNA, and DNA.[8,9] Any of the structural proteins (Spike (S), membrane (M), Envelope (E), and viral RNA

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genome), non-structural proteins (nsp 1–16), and nine accessory proteins could potentially serve as targets of vaccine-induced immunity.[8]

Many candidate vaccines are in various phases of trials, with Food and Drug Administration (FDA) approval and emergency use authorization granted for a few. The WHO started COVAX, the global initiative to ensure rapid and equitable access to COVID-19 vaccines for all countries, regardless of income level, to secure two billion doses of approved vaccine by the end of year 2021.[10] The complete removal of physical and social restrictions across the world will depend upon the equitable access of vaccines and the effectiveness of vaccination programs used by the countries.

Although there are other social, programmatic, and equity issues in such an extensive vaccination program, this article will limit itself to a summary of the approved vaccines in terms of its scientific background, development, immunological response, efficacy, and adverse events.

Vaccine candidates for COVID-19

As of 18 February 2021, at least seven different vaccines across three platforms have been rolled out in countries with vulnerable populations in all countries at the highest priority for vaccination.[11] World's first COVID-19 vaccine Sputnik V was registered and approved for use by Russia on 11 November 2020. The US first COVID-19 vaccine approved for emergency use authorization by the FDA was the Pfizer vaccine, followed by Moderna.[12] The first vaccine to receive emergency use validation by the WHO was Pfizer/BioNTech vaccine.[13] The WHO has given emergency use validation for three vaccine candidates (Pfizer and AstraZeneca [Korea and Indian versions]). As on 17 June 2021, more than 2.47 billion doses have been administered across the 180 nations worldwide.[14]

In India, two vaccines were given emergency use authorization by the Drugs Controller General of India (DCGI) on 03 Jan 21. Vaccination drive using these two vaccine candidates, Covishield and Covaxin, was started on 16 Jan 21 in a phased manner with three crore (30 million) healthcare workers and frontline workers among the top priority group. Table 1 gives an overview of few approved vaccines.

Covishield and Covaxin

Covishield and Covaxin were given emergency use approval in India on 03 January 21.[15] Covishield is an adenovirus vector—nonreplicating virus vaccine, and Covaxin is a viral inactivating vaccine. Both Covishield and Covaxin have shown promising results in preclinical studies[16,17] In phase I and II trials, Covishield (ChAdOx1 nCoV-19) has shown both humoral and antibody response and acceptable safety profile.[18] The ongoing phase three trial has also been shown to have a good safety profile and efficacious (70.4%) in the interim analysis.[19] Covaxin also has acceptable safety and immunogenicity profile in phase 1 trial.[20] The interim analysis of phase three trial found the vaccine efficacy to be 78% (95% CI: 61-88) against mild, moderate, and severe COVID-19 disease.

Table 1 – Overview: COVID-19 vaccines.

Characteristic	Sputnik V	AZD1222 (ChAdOx1nCov19)	Moderna COVID19	Pfizer-BioNTech	COVAXIN	CoronaVac
Type of vaccine	Recombinant weakened nonreplicating human adenovirus vector with spike protein in two components (rAD5, rAD26)	Recombinant spike protein of SARS-CoV-2 carried in chimpanzee adenovirus (weakened and nonreplicating)	It is an mRNA vaccine.	It is an mRNA vaccine that codes for the virus spike protein and is encapsulated in a lipid nanoparticle	It is an inactivated vaccine made by Bharat Biotech	Inactivated virus vaccine developed by a Chinese biopharmaceutical company.
Efficacy	91.4%	90%	94.5%	About 95%	60–70%	50.4% in late-stage trials in Brazil and 91.25% in Turkish trials
No of doses	2 (days 0 and 21)	2 (days 0 and 28)	2 (days 0 and 28)	2 (days 0 and 21)	2 doses, 4 weeks apart	2 (days 0 and 28)
Temp requirement	2–8 C	2–8 C	−20 C	−70 C	2–8 C	2–8°C
Remarks	Dr Reddy's Labs, Hyderabad, is conducting phase 3 trials in India with Sputnik V	In India, the Serum Institute of India prepared the vaccine named Covishield. Mass vaccination drive with this vaccine already started in India on 16 Jan 21	It was authorized by the FDA for emergency use authorization (EUA) on 18 Dec 20	It was sent to the FDA for possible EUA on Nov 20 and authorized on 11 Dec 20	First indigenous COVID-19 vaccine developed in collaboration with the ICMR. Approval for emergency restricted use in India by DCGI-CDSCO on Jan 2021	Emergency approval given in several countries including Brazil, Indonesia, and Turkey.

DCGI, Drugs Controller General of India; CDSCO, Central Drugs Standard Control Organization; ICMR Indian Council of Medical Research.

Since 16 January 21, more than 56 million doses have been given, including Covishield and Covaxin.[21] The distribution of the vaccines used in India is not provided. However, the majority (90%) of the doses are likely to be Covishield.[22] The majority of the side effects have been reactogenic.

Pfizer-BioNTech and moderna (mRNA-1273) vaccine

The Pfizer-BioNtech and Moderna vaccines are the first mRNA vaccine to receive emergency use authorization on 11 December 20 and 20 December 20, respectively.[23] However, mRNA technology is not new. Cancer research has previously used mRNA to trigger the immune system to target specific cancer cells.[24] The platform manufacturing cell lines and clinical-grade subunit protein typically takes years, whereas it takes only a few weeks to produce nucleic acid vaccines.[25,26] In addition to the advantage in reducing the time frame of manufacture, mRNA vaccines are very potently immunogenic and known to elicit humoral and cellular immunity.[27,28] However, limited production capacity and relatively stringent cold chain requirements preclude its wider availability and acceptability in all countries, especially in lower middle-income countries.[29]

Both the vaccines have a lipid-based nanoparticle (LNP) carrier system to deliver in vivo. Encapsulated mRNA vaccine expressed the prefusion stabilized spike glycoprotein.[30] As of 28 February 2021, more than 35 million doses of both vaccines have been administered in the USA alone.[31] The safety of these vaccines has been monitored closely. The vaccines have shown reactogenic side effects equal to placebo. However, anaphylaxis reaction has been noted with the incidence of 1 in 100,000 doses, which is ten times than with previously known vaccine, which has been attributed to polyethylene glycol in LNP.[23]

Janssen vaccine (AD26.COV2.S)

The Janssen vaccine is a recombinant, replication-incompetent adenovirus serotype 26 vector (Ad.26.COV2.S or JNJ-78436725) encoding a full length and stabilized SARS-CoV-2 spike protein and is formally approved for single dose.[32,33] The interim results of phase 1–2a trial showed acceptable safety profile and immunogenicity profiles to support further development.[34] The results of interim analysis of its phase 3 ENSEMBLE Trial among 43,783 participants have shown 66% efficacy overall at preventing moderate to severe COVID-19, 28 days after vaccination.[35] Janssen's single-dose vaccine candidate is estimated to remain stable for 2 years at −20°C (−4°F) and for at least 3 months at temperatures of 2–8°C (36°F–46 F).[35]

Sputnik vaccine

It is a combined vector vaccine. The vaccine is based on rAd type 26 (rAd26) and rAd type 5 (rAd5)—both of which carry the gene for SARS-CoV-2 full-length glycoprotein S (rAd26-S and rAd5-S). The use of two varying serotypes is intended to overcome any preexisting adenovirus immunity in the population. The two variants of the vaccine are administered intramuscularly separately at a 21-day interval. The vaccine was rolled out after the phase I/II trial on August 20. The results of the trial showed that the vaccine is safe and highly immunogenic in healthy participants.[18]

The phase III trial of the vaccine started at 25 hospitals and polyclinics in Moscow, Russia, on September 20. Participants (0.1%) in the vaccine group and 1.3% of participants in the placebo group were confirmed to have COVID-19 after 21 days of the first dose. Vaccine efficacy was estimated as 91.6% (95% Confidence Interval (CI): 85·6–95·2), and 94% of the reported adverse events were mild. Serious adverse events were reported in 0.3% of participants in the vaccine group and 0.4% participants in the placebo group, but none were considered associated with vaccination.[36,37] The Sputnik V vaccine development has been criticized for haste, but the vaccine has shown efficacy in all phase I, II, and III trials.[38]

As per claims, the vaccine has been administered to more than 2 million people worldwide and was registered in more than 25 countries. As of February 2021, vaccination with Sputnik V has started in the following countries: Bolivia, Algeria, Kazakhstan, Turkmenistan, Palestine, the UAE, Paraguay, Hungary, Armenia, Bosnian Serb Republic, Venezuela, and Iran.[39]

Other COVID-19 vaccines

As per China's coronavirus task force, it has 13 vaccines involved in clinical trials. Among them, about five went in phase III clinical trials.[40] The current front runners among the Chinese vaccines are Sinovac, Sinopharm, and CanSino. While Sinopharm and Sinovac have whole inactivated virus vaccines with alum as an adjuvant, CanSino has used a non-replicating version of adenovirus-5 (Ad5) as a 'vector' to carry in the gene for the coronavirus spike protein.[41]

The vaccines from Beijing Institute affiliated with the state-owned China National Pharmaceutical Group (Sinopharm) were approved for use by the general public by China's medical products regulator in December 2020. In contrast, the Sinovac Biotech COVID-19 vaccine has been approved recently in Feb 2021 and marks the second vaccine approved for public use in China.[42]

Despite the lack of publicly accessible data, China had commenced a programmatic rollout of homegrown COVID-19 candidate vaccines. Sinopharm's vaccines were the first among the Chinese vaccines to begin widespread human trials, starting in mid-July in the United Arab Emirates, while Sinovac (China) has partnered with Butantan (Brazil) and Bio Farma (Indonesia) for overseas trials of their vaccine.[43]

Sinopharm has announced an efficacy of 79% for shots developed by its state-owned unit, China National Biotec Group Co. Ltd. The Sinovac vaccine CoronaVac was well tolerated and induced humoral responses against SARS-CoV-2 in phase I/II trial.[39] Sinovac multicountry phase III efficacy trials in overseas countries have announced efficacies varying from 50% to 91%.[40] CanSino's late-stage trials for its experimental coronavirus shot have shown an efficacy rate of 65.7%

to prevent symptomatic cases.[41] However, these data from the phase III trial have not been published or peer reviewed.[42–44] China has also rolled out single jab vaccine Ad5-nCoV COVID-19 which provides immunity for six months.[44]

Newer developments

The single-dose vaccine would become available, which would act as a boost to the vaccination campaign.[34,44] A single-dose intranasal vaccine would stimulate a broad immune response and probably might prevent transmission also. These vaccines are in phase/II trials.[45,46] Another vital aspect of vaccination is the virus's mutation and the possibility that these mutations may escape immunogenicity developed by vaccine and reduce existing vaccines' efficacy. Hence, the composition of the vaccines may need to be changed to protect against new mutants.[47]

Conclusion

The development of the COVID-19 vaccine in such a short period is a true testimony to the technology and scientific development which had taken place over the years. The multiple vaccine candidates with multiple platforms have been developed. This editorial describes the present status of the vaccines and describes the available one which has been given emergency use authorization. Since the vaccines have been given emergency use authorization during a pandemic, the data about rare and long-term effects are lacking. The need for robust monitoring and postvaccine surveillance is essential to identify the vaccines' full beneficial and adverse effects. Newer nasal vaccines may prevent transmission also. There is need to be alert for viral mutants as these mutations may escape immunogenicity.

Disclosure of competing interest

The authors have none to declare.

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