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Short Review

COVID – 19 Vaccines: Sliver of Hope in the Face of the Pandemic

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BACKGROUND

The world woke up to a dreadful pandemic in the year 2019-20, and before we can take action the dreadful virus quickly caught the entire globe within its paw. Since the first reported incident, we have been trying to come out of this wildfire. The world came together for once, trying to find out a way with vaccines against the virus as the only ray of hope. Before the pandemic set in, we already knew about the structure and functioning of these Coronaviruses due to the previous outbreaks of Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS). This pre-existing information fuelled the development process with more pace.[1] In the beginning the primary goal for a COVID-19 vaccine was to prevent progression of the disease towards severe form.[2]

Phased distribution has been done in countries in a manner where higher priority corresponding to increased risk of receiving the infection such as Health Care Workers, and increased risk of complications such as elderly persons.[3]

As of the date 18/09/2021, worldwide 5.92 Billion doses of COVID-19 Vaccines have been administered (Based on reports from National Public Health Agencies)4. And in India around 597,205,296 doses have been administered. Observational and Case control studies have been come in to use to asses Real-World Vaccine Effectiveness, as multiple COVID-19 vaccines have been authorised.[5] There is an ongoing study which is investigating the long term effect of mRNA vaccines in protection against the SARS-Cov2.[6]

CLINICAL RESEARCH

As of today, there are around 22 potential vaccines which have received authorisation for use by National Agencies. Around 6 vaccines are authorised for Emergency or Full Use by Stringent Regulatory Authority, out of these six, five of them are in phase IV. In total 330 vaccines are in different stage of development , out of them 102 are still in clinical research phase, with Phase I and Phase II trials comprising of 30-30 each, Phase II trial including 25 and 8 vaccines in Phase IV development.[7]

Phase II trials showed promising results for several vaccines with efficacy touching 95% in preventing COVID-19 infection, especially symptomatic infections. The table below enlists various vaccines with their type.[8,9]

TYPES OF VACCINES

There are in total 9 platforms serving as a base in development of COVID-19 Vaccine.[10]Most of these bases target the Spike Protein of the SARS-CoV-2 and its variants as the primary antigenic structure.[11] Newer bases also involve Nucleoside-Modified Messenger RNA and DNA, Non Replicating Viral Variants, rcProteins, Peptides and Live attenuated and Inactivated Viruses.[12,13,14]

Table -1; Various COVID-19 Vaccines

Type Of Vaccine	*Manufacturer*
DNA Vaccine	ZyCoV-D
RNA Vaccine	Pfizer-BioNTech, Moderna
Viral Vector	Oxford-AstraZeneca, Sputnik V, Jansen
Conventional Inactivated	Chinese Academy of Medical Sciences, BBIBP-CorV, Covaxin, CoronaVac, CoviVac, COVIran Barekar, QazVac, WIBP0CorV, FAKHRAVAC, Minhai-Kangtai
Protein Subunit Vaccine	EpiVacCorona, MVC-COV1901, Soberana 02, Abdala, ZF2001

1. RNA Vaccines

Pfizer-BioNTech, Moderna are examples of RNA vaccines. These vaccines act as a messenger RNA, which cause the cells to build the Spike Protein, thus teaching the body how to identify and destroy such pathogen. This delivery is done but Lipid Nanoparticles.[15] Efficacy is around 85-95%. [16]

2. Adenovirus Vector Vaccines

They are examples of Viral Vector Vaccines using adenovirus as a DNA container.[17]Oxford-AstraZeneca, Sputnik V, Janssen vaccines are such examples. Efficacy is around 66-81%[18]

3. Inactivated Virus Vaccines

These agents are grown in culture and killed with heat of Formaldehyde; hence they loose infective strength, while still being useful in developing an immune response. Indian Covaxin, Chinese CoronaVac and Iranian COVIran Barekat are such examples.

4.Protein Subunit Vaccines

They consist one or more antigenic structure but excluding whole pathogen particles. It can be any molecule being a fragment of the pathogen[19] EpiVacCorona, MVC-COV 1901, Novavax Covid-19 are such examples.

5. Intranasal Vaccines

These vaccines specifically target mucosal immunity comprising in nasal mucosa, which often acts as an entry point for the virus into the body. They stimulate the immune response in the nasal cavity (Such as IgA).[20]

6. Other Types

Other types of vaccines include Multiple DNA Plasmid Vaccines, Lentivirus Vaccine, Vesicular Stomatitis Virus with Spike Protein etc.[21,22,23]

VARIANTS OF SARS – COV – 2

Availability of new vaccines is changing the landscape of natural host immune system (i.e. Humans) correlating with SARS-CoV-2 Virus.[24]Newer clinical trials are indicating that vaccines targeting the initial strains of the virus, has reduced efficacy for the newer mutant strains.[25]This is phenomenon is mainly discussed in a study done by Simon A. Rella, et al. stating that emergence of a resistant strain has higher chances in a population where there is rapid transmission amongst already vaccinated individuals.[26]

ALPHA VARIANT

The B.1.1.7 variant was the preliminary variant of SARS-CoV-2. Antibody neutralisation was highest with the most commonly distributed vaccines (Moderna, Pfizer-BioNTech, CoronaVac, Covaxin)[27]

BETA VARIANT

Scant research is available for the different variants and vaccine efficacy but, the available limited data shows that efficacy of the initial vaccines is reduced for the beta VAIRANT (B.1.351)[28]Pfizer announced that the neutralising capability of their vaccines had a substantial reduction (2/3rd) for the beta lineage.[29]

GAMMA VARIANT

CoronaVac and BBIBP-CorV seems to retain efficacy for the Gamma (P.1) variant, which was first introduced in Brazil. It; however seems to evade vaccination with Pfizer-BioNTech vaccine.[30]

DELTA VARIANT

The Delta variant was first discovered in India around October 2020, which was numbered B.1.617. Till January the infection rate was scant but within 3 more months it spread to at least 2-

new countries escaping Antarctica and South America.[31] This variant is often referred to as "Double Mutant" as the spike protein mutations are related with reduction in neutralization. Public Health England announced the Delta variant as Variant of Concern given the equivalent transmissibility compared to the Alpha Variant.[32]

HETEROLOGOUS PRIME BOOST VACCINATION

Newer studies are coming to light, stating that Heterologous priming can boost immunity against SARS CoV-2.[33] Several European countries and Canada are advising a heterologous second dose to those who received Oxford-AstraZeneca as the first dose.[34]

The Com-COV trial was launched by Oxford Vaccine Group in order to investigate a heterologous prime boost vaccine course of available vaccines. This group is conducting two Phase II studies named: Com-COV & Com-COV2 and an Adolescent study named Com-COV3.[35]

First Dose	Second Dose	Schedules	Study and Current Phase
Oxford-AstraZeneca & Pfizer- BioNTech	Oxford-AstraZeneca & Pfizer BioNTech	0-28 Days 0-84 Days	Com-COV; Phase II[36]
Oxford-AstraZeneca or Pfizer-BioNTech	Moderna / Novavax	0-56-84 Days	Com-COV2; Phase II[37]

SIDE EFFECTS

Vaccines are injected intramuscularly and hence the side effects related to Trauma such as pain, rash, soreness and often inflammation at injection site is fairly common. Hypersensitivity reaction towards the vaccine has been reported around 1:1000 people, with possibility of causing serious anaphylaxis.[38,39]

EMBOLIC AND THROMBOTIC EVENTS

The Janssen vaccine did report a rare incident of blood clot formation along with low platelets (Thrombosis with Thrombocytopaenia; TTS) with incident rate of around 7/10,00,000 for women aged 18-49 years.[40] After the Pfizer-BioNTech or Moderna Vaccination a rare case of Myocarditis and Pericarditis has also been reported.[41] However recovery from such incidents are quick when adequate rest and treatment is incorporated.[42]

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