Review Article

REVIEW OF DIFFERENT VACCINES AND VACCINATION CAMPAINGS AGAINST COVID AROUND THE GLOBE AND INDIA

ABSTRACT:

BACKGROUND: Corona virus is caused by beta variant of coronavirus, occurred as an unexpected breakout from the city of Wuhan , spreading across borders in no time. A large number of measures like imposing strict curfews, lockdowns, avoidance of public gatherings, home isolation, quarantine etc. have been imposed in the nation to curb the disease transmission, but none of the measures were enough to stop the viral transmission. The only efficient measure to stop the transmission of virus is developing herd immunity by the use of vaccines. As known from the past experiences vaccines take a long time to get approval, but many COVID vaccines have received emergency approval for public use.

SUMMARY: Vaccines, by creating herd immunity in the population, are the most efficient strategy of limiting the epidemic. Vaccines are the most cost-effective method of preventing infection transmission. Vaccine development typically takes several years, however due to significant mortality; numerous vaccines against COVID-19 have obtained emergency approval**.**

CONCLUSION: Most of the vaccines developed today or in trial aim at targeting the S protein or the RBD region. There has been remarkable success in development of COVID-19 vaccine since the registration of first case on January 10-2020.Mortality and morbidity associated with the disease are increasing day by day and hence temporary measures like lockdown and stay-at-home strategy would not suffice for long. A large number of vaccination campaigns have been launched around the globe. They aim at reducing the incidence of the disease and henceforth the associated mortality.

KEYWORDS: COVID-19, Immunity, Pandemic

INTRODUCTION:

COVID-19, a global pandemic , is still spreading over the world, posing major concerns to public health and economic stability. Developing safe and effective vaccines is the need of the hour to protect the world population and economic stability. The vaccine candidates in India that are undergoing clinical trials are among the leading and most advanced products in the world. Some of the local Pharmaceutical corporations have partnered with vaccine developers headquartered in other countries. for clinical trials as well as large scale manufacturing of vaccines. Helper T (Tc) cells are activated by ingestion of specific viral particles attached to antigen presenting cells. It then activates other immune responses such as B cell and production of cytotoxic T (Tc) cells. B cells make antibodies that stop the virus from invading cells, whereas

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Tc cells recognize and kill the virus. Complete understanding of the etiology, pathophysiology, communicability and affinity is essential for development of vaccines in principle.(1)

SARS-CoV-2

Corona virus have a helical nucleocapsid and are enclosed positive-sense single stranded RNA viruses. The strain currently affecting the world is a beta coronavirus. Although it is unknown how the virus initially infected people, bats were known to transmit virus to human causing outbreak in the Wuhan city of China. Majority of patients complained of shortness of breath along with cough, fever, myalgia and tiredness. The laboratory findings in the active phase of disease includes high c-reactive protein(CRP), lactate dehydrogenase(LDH), lymphopenia and reduced albumin. Longer prothrombin time and elevated D-dimer values were observed in the patients admitted in Intensive Care Unit (ICU's). Patients with comorbidities like hypertension, cardiovascular diseases and diabetes have a more fatal course of illness. The S-protein, a key trimeric envelope glycoprotein produced on the virus's surface, is the major target protein for the vaccines as it is responsible for buildup of virus inside host cell by attaching to it. The S-protein consists of 2 subunits: S1, responsible for binding to receptor, and, S2 regulating membrane fusion. The S protein by attaching the cell and viral membrane undergoes major alteration.

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The S1 subunit, which consists of an N-terminal domain and a receptor-binding domain(RBD), is principally responsible for the variations in the S protein. A major concern about the SARS-CoV-2 infection is that a large majority of individuals become the asymptomatic carrier of the disease and have the potential on unknowingly transmitting the infection to multiple people. (1)

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COVID-19 VACCINE DEVELOPMENT

Developing a low-cost effective vaccine is essential for mitigating the lethal COVID-19 pandemic. Several attempts are ongoing to develop vaccine at the earliest since the appearance of virus. As reported in December 10, 2020 about 214 potential vaccine candidates were undergoing trials.

The initial stage of vaccine development is an exploration phase that involves the search of various natural and synthetic antigens that would act as vaccine candidate to control and prevent the disease. This phase consist of laboratory bench research and modeling using technology to derive potential candidates. The most initial trials are done using cell-culture and tissue-culture system followed by inoculation in animals to determine the safety, immunogenicity and its ability to produce a sufficient amount of immune response are the second stage. Once animal safety, immunogenicity, and efficacy have been proven, human clinical trials are conducted, in which antibody titers and toxicity are tested in relatively small group of people before being tested in large groups. (2)

Phases of vaccine development

Phase 1 - Safety: The vaccine is given to humans for the first time in this stage. A small population of healthy and immunocompetent individuals are selected, the vaccine is given, dose is calculated and adverse effects are looked for in the form of immunological response.

Phase 2 - Expanded Safety: Hundreds of people are administered the vaccine, which is divided into separate groups based on demographics (for example, elderly vs. young). This phase usually tests the safety of vaccine, determines the dose to be administered to general population and time interval between two doses. This phase ensures that the vaccine is both safe and immunogenic, as well as determining the optimum dose for next phase.

Phase 3 - Potency: In this stage large scale trials are done in thousands of volunteers to determine the efficacy of vaccine. The patients will be monitored for reduction in disease incidence in vaccinated groups compared to placebo groups and this is termed as vaccine effectiveness (VE).
With the completion of human trials and ensuring the safety and potency of the vaccine, it is taken to the next step:

Review and Approval: Various organizations, like the US Food and Drug Administration (FDA) or the European Medicines Agency (EMA) in the EU, must normally assess findings before deciding whether the vaccine is suitable for approval. This procedure usually takes one to two years, so some vaccines are licensed for emergency use.

Surveillance during production and thereafter: Post large scale manufacture and marketing to general public, effectiveness of the vaccine is assessed. They also keep track of any negative effects of concern when the vaccine is widely used.(3)

COVID-19 VACCINE CANDIDATES IN INDIA

The Serum Institute of India's Covishield

Pune-based Serum Institute of India (SII) has signed agreements with a number of companies. Oxford-AstraZeneca, Codagenix, and a few more among the makers are Novavax. The Oxford-based company is now producing vaccine on a massive scale. In India, now marketed as "Covishield," and it has stockpiled approximately 50 million doses. After January 2021, the company plans to produce 100 million doses per month. SII plans to increase its capacity to 2 billion doses per year.

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Studies for the next phase were started across 14 centers in India under the collaboration of SII and ICMR. Competitive study between the covisheild produced indigenously versus the conventional Oxford vaccine were carried out to determine the potency of Indian vaccine in comparison to original vaccine. 1600 patients were enrolled to participate in phase II/III trial, the patients essentially being at least 18 years old. Out of the total 1600 participants 400 were given Coviesheild or Oxford-ChAdOx1 in the ratio of 3:1 respectively as a part of cohort of immunogenicity. The remaining 1200 patients in the safety cohort were given Covishield or Placebo in a 3:1 ratio. As observed the efficacy of vaccine was seen to be equivalent of prior trials conducted outside of India in terms of safety and immunogenicity. (4)

Covaxin by Bharat Biotech Ltd

In collaboration with the Indian government, CovaxinTM, India's first native COVID vaccine was designed and sold in conjugation with National Institute of Virology of the ICMR. It is one

of the company's two vaccines, which are currently in clinical studies, being stored in an "at-risk production and stockpiling"licence".CovaxinTM is a virus vaccine that was created in Vero cells. Alhydroxiquim-II is mixed with the inactivated virus (Algel-IMDG) imidazoquinoline was chemosorbed onto an aluminium hydroxide gel as an adjuvant to potentiate the immune response and immunity for longer duration.

The initial researches of the vaccine on animals such as mice, rabbits, hamsters and other animals proved to be producing good immune response. The company has exchanged data with the drug regulatory agency. As per the results demonstrated by trials the vaccine is proved to be safe and provides good immune response.(4)

Cadila Healthcare's ZyCoV-D (Zydus Cadila)

The Department of Biotechnology is supporting the development of next native coronavirus vaccine, by Cadila Healthcare in Ahmadabad, ZyCoV-D which is built on the novel plasmid DNA vaccine technology. Public usage of plasmid DNA technology is not permitted. Plasmids are a type of genetic material that can be employed as a vectors for delivering DNA with viral antigens directly in the recipient's system. Antigen of the pathogen is cloned into recombinant plasmid DNA.

Unnamed COVID vaccine by Biological E. Limited

The vaccine is currently undergoing phase I/II clinical trial in India being made by Dynavax Technologies Coropration and Baylor College of Medicine. .By February 2021, the findings from these clinical trials should be accessible. The immunization regimen consists of two doses (of the same potency) provided via intramuscular injection 28 days apart for each trial participant. BE's COVID-19 vaccine, which was developed locally but is yet unknown, has also got regulatory approval in India for clinical trials. The drug studies' specifics have yet to be revealed but reports suggest that vaccine might be launched by September-end.

Dr. Reddy's Laboratories' Sputnik V

It is a human adenovirus-based two-vector viral vaccination. Ad5 and Ad2618 adenoviruses are used in Sputnik V. Efficacy of 91.6% has been recorded after two doses of the vaccine. Antibody titers produced are comparatively higher compared to other native vaccines in India. Anti-spike antibody responses were generated in 94 percent of vaccinees, with 90 percent exhibiting WT virus-neutralizing potential. Importantly, seropositive volunteers who were administered first done of the vaccine had quick and vigorous immune response, with antibody levels better than those in seronegative volunteers vaccinated with both doses.(5)

Various Platforms for COVID-19 Vaccine Development

DNA Vaccines

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The S protein of coronavirus is the major protein antigen used for making DNA vaccines. DNA vaccines are extremely stable at room temperature with easy storage and distribution system. There are easy to manufacture in vitro so are more accessible to naïve areas of the nations . Low immunogenicity was observed with the DNA vaccines were delivered using needles without use of other delivery tools like adjutants. Various recent delivery systems like electroporators or gene gums are used to boost up the immunogenicity during mass vaccination. A few examples of DNA vaccines include: Inovio Pharmaceuticals, Symvivo in Canada, Cadila Healthcare Limited in India.(6)

RNA-Based Vaccines

Moderna/NIAID

Moderna, a Cambridge, Massachusetts-based venture, was also researching mRNA-1273, an mRNA-based vaccine. Given in two shots 28 days apart , immunocompromised individuals may require 3 doses. The adverse effects associated with the vaccine like rise of temperature, chills are usually noticed post 2nd dose. As proven in trials the vaccine is 94.1% efficacious in preventing clinically proven COVID-19 infection in recipients aged 18 years or more vaccinated with both doses. In clinical trials, the immunization was quite efficacious at prevention COVID-19 in patients of every age, gender, region, culture as well as elderly with various co-morbidities.(7–9)

BioNTech/Fosun/Pfizer

It is an mRNA-based vaccine, being developed by BioNTech in collaboration with an American corporation Pfizer,. BNT162 is a vaccine candidate that combines modified mRNA as well as a trimerization domain generated from T4 fibritin to increase immune response. The vaccine was 95% effective in preventing COVID-19 infection as observed in phase III trials within first 28 days itself. Determining the dose, timings, budget of the vaccine is a major problem because of insufficient data available on the time span of immunity provided by the vaccine. Latest reports suggest that the vaccine provides good immunity to elderly over 65 years of age with co-morbidities .
Other examples of RNA vaccines include : Cuevac by Germany, Arcuturus etc. (10)

Vaccines with non-replicating viral vectors

University of Oxford/AstraZeneca

Currently in the phase of clinical trials and showing a good antibody titer ChiVaxAZD1222,previously known as ChAdOx1 is a viral vector vaccine produced by University of Oxford in partnership with AstraZeneca. (11)

CanSino Biological Inc.

It is a one-shot vaccine. The Chinese military and a Tianjin-based biotech company collaborated on this project. Its efficacy is lower as compared to Pfizer and modrena but a candidate has been added to one-shot vaccine list. Its advantage includes that candidates from CanSino is easier to keep and do not require patients to come at allotted time for the second dose, which is difficult to ensure in developing nations. It is about 65.7% efficacious in staving off symptomatic COVID-19. (12)

LIVE ATTENUATED VACCINE

Produced by traditional method, these vaccines are highly efficacious and produce strong and long-lasting immunity. The virus is repeatedly replicated in cultured cells and then virus particles with weekend capability and reduced virulence are selected. These vaccines should be used carefully in immunocompromised individuals due to risk of live viruses. Some examples of live-attenuated vaccines are: Codagenix

COVID-19 VACCINATION CAMPAINGS ACROSS GLOBE

The coronavirus created havoc worldwide. It is associated with high mortality and morbidity thus making it imperative for the nations to develop vaccines as soon as possible. A large number of precautionary measures were taken by the Govt. like imposing nation-wide lockdowns, curfews, wide-scale sanitization etc. but none of the measures were completely successful in stopping the spread of deadly virus. The production of vaccines is a long process and can take many years, but many vaccines received emergency approval due to high mortality associated with the disease. Next major step was to encourage people to take vaccine among the prevalent misinformation, especially in a developing country like India. Herd immunity is the goal of vaccination efforts. The best way to deploy the vaccine is still up for dispute. Some governments have large-scale deployment plans. Morocco intends to vaccinate up to 80% of the people. A large number of mass vaccination campaign were launched by the govt. of different nations like Operation Wrap Seed by US govt., primarily targeting high risk groups like health-care workers, sanitization workers, elderly population with co-morbidities, police personnel etc. Bonuses for receiving voluntary immunizations have been offered, including, for example, monetary rewards. Qantas Airlines just declared that the vaccine will be required for all customers.(13)

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In the COVID-19 era, what are the challenges and opportunities for mass vaccination centres?

SARS-CoV-2, a novel extremely infectious corona virus, surfaced in the Wuhan city of China at around the end of 2019, producing an outbreak of unexplained viral pneumonia. The virus was highly contagious and crossed borders within no time. Despite our best efforts, COVID-19's growth in Europe has pushed healthcare institutions to their breaking point from fall 2020 and North America, emphasizing the need for a mass vaccination thus developing hed immunity. Ensuring mass vaccination, high immunity, equitable distribution is still a problem because it requires huge amount of trained man power, funding and resources. A major concern with vaccines is its uninterrupted supply, maintenance of cold chain in terms of temperature control

and storage. In developing countries like India loss to follow up for 2nd dose is also a major concern .(14)

INDIA'S COVID VACCINATION CAMPAIGN

On January 30, nation reported its first COVID_19 case in a 20-year aged women returning from Wuhan , to the Southern state of kerala. Very soon the virus had spread to whole of the country. Most of the patients presented with the complains of fever, chills, sore throat, and less commonly with loose stools, headache, loss of sense to smell and taste. As of now, India has reported 3.26cr cases in total with 4.36L deaths. (15)

'On January 16, 2021, India officially launched its COVID-19 vaccination campaign. The Drug Controller General of India (DCGI) certified the Oxford–AstraZeneca vaccine for emergency use on January 1, 2021. (Local trade name "Covishield"). BBV152 (trade name "Covaxin"), a native vaccine produced by Bharat Biotech in collaboration with the ICMR and the National Institute of Virology, received an interim emergency use authorization from the DCGI on January 2. The first phase of vaccination started targeting 30 million of healthcare and frontline workers. The second phase of vaccination aimed at elderly above 60 years of age, with co-morbidities along with health care workers that were not vaccinated in the first phase. The registration for vaccination was done online through Aarogya Setu app and Co-Win app later in this phase. Third phase of this vaccination campaign began on May 1, extending vaccines availability to everyone above 18 years of age. On April 12 Russia's sputnik v with 91.6% efficacy was approved for emergency use in India. Some of the key studies related to vaccination and Covid-19 were reviewed (16-21).

Vaccine Maitri launched on January 2021 by the government of India aimed at exporting vaccines to neighboring nations like Bangladesh, Bhutan, Maldives, Nepal etc. Till date India has administered 61.2Cr doses of COVID vaccine with 35.5% population receiving first dose while 10.5% population being fully vaccinated(22).

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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