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THE COVID-19 VACCINES: HOPE OF WORLD

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ABSTRACT

A coronavirus disease pandemic (COVID-19) is worldwide problem with no sufficient evidence of a declining pattern caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It is mainly believed that normal human life is impeded by securing a reliable vaccine strategy. Many countries have created vaccine for effective treatment with COVID-19. An effective vaccine is needed to protect humans' life and to mitigate the economic and societal impacts of the global pandemic. For standard vaccine development usually requiring several years to complete all total clinical phases. Moreover, vaccine candidates have recently been granted an Emergency Use Authorization. Furthermore, for Pfizer/BioNTech, Moderna mRNA vaccines, and Johnson & Johnson viral vector vaccine all are made by the US and Food drug administration and the AstraZeneca vaccines are made by the oxford university of United Kingdom. Sinopharm by China government have recently granted Emergency Use Authorization to vaccine candidates. and by Indian government COVISHEILD AND COVAXIN made by (Bharat biotech). Here we target to briefly address the current advances in covid 19 vaccine available in world market, reverse genetics system of SARS-CoV-2 and the use of this in development and implement of SARS-CoV-2 vaccines.

Keywords: *Covid 19, vaccine, delta variant, omicron variant, booster dose*

INTRODUCTION

Coronaviruses have been linked to upper respiratory and gastrointestinal infections in a variety of animals species. mild and self-limiting common cold symptoms can be caused by 4 coronaviruses, including 2 alpha coronaviruses and 2 beta coronaviruses. In addition, there are 3 beta coronaviruses known to cause respiratory syndromes with high mortality rates in humans, namely, severe acute respiratory syndrome coronavirus, Middle East respiratory syndrome (MERS-CoV) and severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) responsible for the ongoing pandemic and Coronavirus Disease 2019 (COVID-19) and now days, a new variant of OMICRON is detected with high transability. As the race for the productive, effective and safe vaccine has begun, different strategies were introduced. viral vector-based vaccines, genetic vaccines, attenuated vaccines, and protein-based vaccines are the main vaccine types tested in the clinical trials Over 80 clinical trials have begun; however, only 18 vaccinations have progressed to clinical phase II/III or III, and seven vaccines are now being considered or have been licensed. or have been approved for the emergency use so far. vaccines against all variants of covid 19 have been actively developed. The spike protein has been recognized as the antigenic target for coronavirus vaccines [2].

IMMUNE RESPONSE TO SARS-CoV-2 VIRUS

The immune response affects the severity of the COVID-19 disease. SARS-CoV-2 infection has a control on both innate and active immune responses [14]. It has been represented that SARSCoV-2 enters the body through physical barriers, such as respiratory tract, oral mucous membrane, and conjunctival epithelial tissue. The dendritic cells, macrophages, and neutrophils represent the first line of defense, and their functions could also be promoted by the manufacturing of type I and III interferons by SARS-CoV-2-infected human cells [15]. Active T-cell and B-cell-mediated immune responses are present in COVID-19 illness, but they are inhibited by SARS-CoV-2. In some circumstances, innate immune cells may play a role in excessive inflammation and, as a result, disease progression. Inability to gain control of the infection may result in dysregulated inflammatory responses, which could be fatal. Within 1–2 weeks, immunoglobin M and immunoglobin G antibodies to SARS-CoV-2 were evident, and by 8 weeks, they had started to decline. IgA reaction peaks earlier than IgM response, according to several studies. The antibody response causes the development of neutralizing antibodies against the S protein and the

nucleoprotein in particular. The bulk of recently developed vaccinations also target the S protein molecule. The size of neutralizing antibodies is related to the severity of the disease and the robustness of the T-cell response. T-cell responses were detected in people recovering from mild COVID-19 infection. who had no detectable anti-SARS-CoV-2 antibody responses Although an effective vaccination may not be able to eradicate the SARSCoV-2 virus, it may provide some protection against severe and lethal COVID-19 disease forms Current information on the SARS-CoV-2-immune system interplay, as well as antigen selection, vaccine platforms and adjuvants, vaccination routes, and hence dose regimens, will be incorporated into the vaccine regimen [1].

TYPES OF VACCINES

Inactivated Vaccines

Inactivated vaccines typically based on presenting the type of infective agent with a loss of disease-producing capability. The virus cultivation happens in cell lines that represent a substrate for the manufacturing of large quantities of antigen. Virus multiplication is usually followed by a purification and concentration before to the vaccine inactivation. The majority of licensed human antiviral vaccines contain formaldehyde and beta-propiolactone to inactivate the virus. Multiple doses or adjuvants are needed to attain efficacy of inactivated vaccines. COVAXIN is an inactivated covid 19 vaccine developed by Bharat biotech in association with Indian council of medical research (ICMR) and national institute of virology (NIV) [1].

DNA Vaccines

The genes of corona virus are transfer to the human cells through DNA vaccine. The main principal behind these is translocation of DNA into human cells, where the transcription of an antigen is started and translation respectively. DNA vaccines often use plasmids as vectors. Myocyte or keratinocyte are addressed which is mainly depends on route of administration either it may be (intramuscular, intradermal, subcutaneous. Because of the cross-priming potential, the produced antigens are loaded onto MHC I and MHC II molecules by antigen presentation cells located close to the application site, which can be transfected directly to DNA vaccine in such instances. [7]. The antigens which are manufactured are either released by exosomes or apoptotic bodies which result in a recognition by antigen -presenting cells and further evolvement of humoral or cytotoxic immune responses. Completely Different delivery devices are used to create a robust immune response. Low level of chromosomal integration of extrachromosomal plasmid is used in development of DNA vaccine. Furthermore, the majority of plasmids remain at the site of administration [8].

RNA Vaccines

In early of 1990s, the Messenger RNA (mRNA) vaccine are first tested, but due to the instability of these vaccine, their use was limited [8]. The genetic information is encoded by mRNA to produced antigen and RNA vaccine embark on to production of coronavirus protein in vivo. The in vitro generation of an RNA vaccine includes a reaction of a DNA plasmid template and a recombinant RNA polymerase. To construct a mature RNA sequence, a synthetic cap analogue and a poly(A) tail are added. Various transport mechanisms (such as lipid nanoparticles, nano-emulsions, and cationic peptides) or approaches permitting easier transfection are used to further stabilize the cells (gene gun and electroporation). The beginning of temporary antigen expression in the cytoplasm of the host cells is the basis of traditional mRNA vaccines. Self-amplifying mRNA vaccines, which contain both the genes coding for the targeted antigen as well as the genes required for self-replication, are another platform (mostly RNA dependent RNA polymerase) [9]. Antigen expression is elicited quickly by conventional mRNA vaccines, and the produced antigens elicit both humoral and cellular immune responses [10-13]. A delayed antigen expression may prevail in self-amplifying mRNA vaccines, limiting vaccination efficacy. However, because the self-amplifying mRNA vaccination platform achieves better yields, a comparable level of protection can be achieved at considerably lower dosages [14]. Regarding the safety profiles, the replicons of both above mentioned platforms are not capable of producing viral particles due to the lack of viral structural proteins. Furthermore, neither traditional nor self-amplifying mRNA vaccines are capable of integrating into the host genome. In rabies, influenza, and Zika virus, mRNA-based vaccines were able to elicit the formation of functional antibodies with neutralizing capabilities, and they also represent a viable immunization method in the prevention of COVID-19 infection. [15]. Clinical trials in phase II and phase III are now being conducted to determine efficacy and safety.

Viral Vector-Based Vaccines

Viral vector-based vaccines (VBVs) are manufactured by engineering a viral vector to carry coronavirus genes and slowly replicate in the host cells. Formation of coronavirus proteins and a subsequent immune system activation is result of Replication. Potential viral vectors include a broad spectrum of both DNA and RNA viruses. These viral vectors are manufactured by both replicating or nonreplicating vectors [15]. The preexisting immunity of the host may affect the efficacy of the viral vector vaccine. This can be avoided by the utilization of non-human or rare serotype vectors. The safety consideration includes the potential of viral genes to integrate into the host genome and uncontrolled replication. On the other hand, the high yield production supports the use of VBV particularly in the time of disease outbreaks. In SARS-CoV-2 vaccine development, the most commonly used vectors are the adenoviral vectors, such as Chad Ox [15,16].

NEED OF COVID-19 VACCINES

The effectiveness of active sedation in preventing infection or subsequent infection was thoroughly investigated, and no operators were moved any further. There have been several medications, primarily hydro-chloroquine and on the basis of a large number of prepared, contradicting, and confusing research, resuscitation has been proposed as a series of frenzied efforts to combat COVID-19. These and other medicines can save lives not shut their doors to regularity in the expressed turmoil of the pandemic. It leads us to a specific option of a successful and stable antibody, which must be rendered for as long as all nations and communities influenced by the widespread at fair pricing may envisage and accessible. [6].

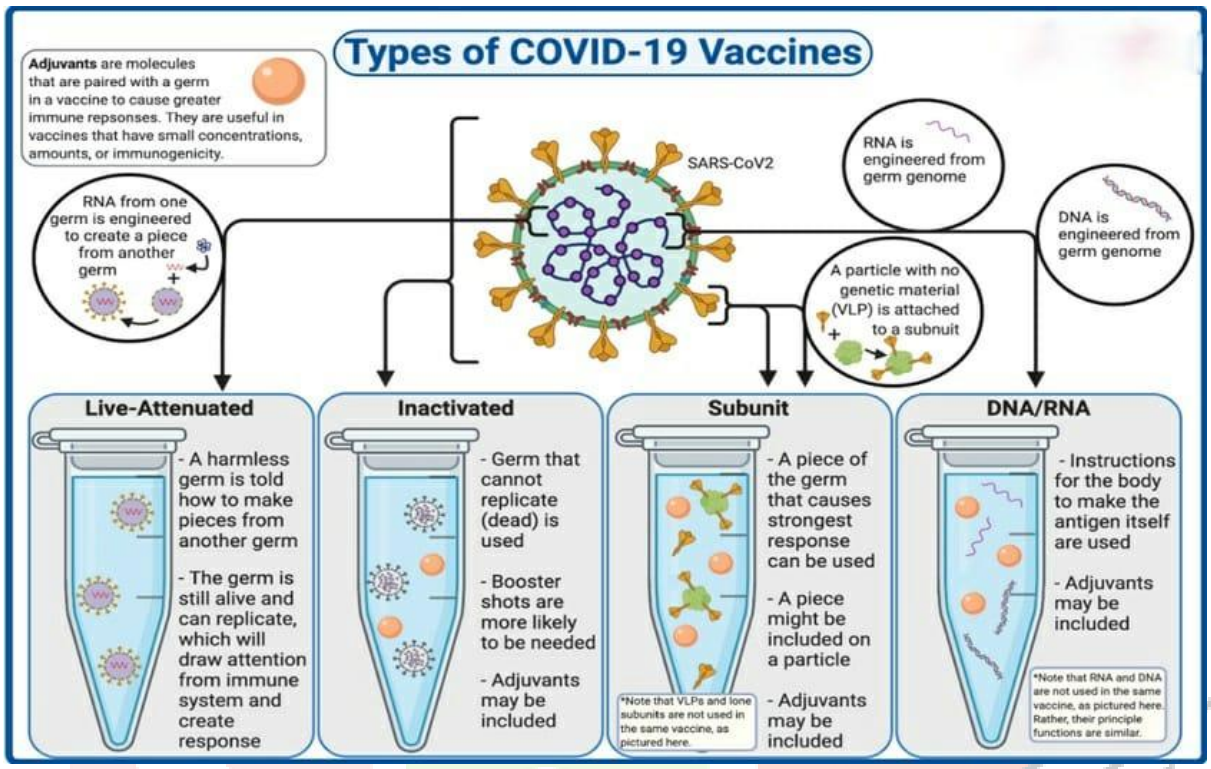

Fig No .1: TYPES OF COVID 19 VACCINE

TABLE NO.1: TYPES OF COVID-19 VACCINE

HISTORY OF VACCINES FOR CORONAVIRUSES

Platform	Candidates in clinical trials and phases	Types of candidates vaccine	Target antigen	Single /multiple dose	speed	Immune response	Advantages	Disadvantages
DNA	In vivo Pharmaceuticals - phase ½	DNA plasmid vaccine with electroporation	Spike protein	Multiple Fast	Fast	Both humoral and cellular	Electroporation generates a robust immune response - Made using genetic sequence and does not need to be cultured	-Although deemed to be safe, electroporation can be complicated and potentially problematic. -No DNA based vaccine has been previously produced
RNA	Moderna/NIAID - BioNTech/Fosun Pharma/Pfizer -	Lipid nanoparticle [LNP]-encapsulated mRNA 3 LNP-mRNAs	Spike protein Spike protein		Fast	Both humoral and cellular	Made using genetic sequence and does not need to be cultured	-LNP is temperature sensitive - Ability to manufacture large scale unknown -No RNA based vaccine.
Non-replicating viral vector	AstraZeneca/ University of Oxford - phase 3 CanSino Biological Inc./Beijing Institute of Biotechnology -	AZD1222 Adenovirus type 5 vector	Spike protein Spike protein	Single	Medium	Both humoral and cellular	-Can be manufactured large scale -Safe and effective immunologically as shown with Ebola	Pre-existing immunity could hamper clinical use and reduce immune response
Inactivated	Wuhan Institute of Biological Products/Sinopharm - phase 3 Beijing Institute of Biological Products/Sinopharm - phase 3	Inactivated	Whole virus	Multiple	Medium	Mostly humoral	-Pathogen is killed and hence, no risk of reversion	Risk of vaccine-enhanced disease - Usually produce a weak immune response

Table no. 1: Types of covid 19

Coronaviruses enclose a single-stranded positively responsive RNA genome with an expanding, helical nucleocapsid (N) and an external surface made up of a protein grid M, a protein E, or S proteins. The area for the receptor retention (RBD) that can officially be converted into the angiotensin-converting enzyme 2 (ACE2) and into the cell is included in the S protein, which is normally trimeric. In SARS-CoV, all of the essential proteins, and possibly a main vaccine antigen target, S protein has been shown to elicit a neutralizing counteracting agent. The advancement of coronavirus vaccinations has been proven to be problematic. Coronavirus antibodies were immunogenic and mainly ineffective in preventing infection in animal models that mimicked human disease. However, there is concern that, as with a typical coronaviral disease, inoculation may not be possible for long-term susceptibility, and reinfection may be possible. In several cases, disease associated to vaccine has improved [5].

RNA BASED VACCINE

Moderna/NIAID

Moderna, a Cambridge, Massachusetts-based startup, is also working on an mRNA-based vaccine called mRNA-1273. The spike protein is coded for in the mRNA vaccine, so when it is delivered into the body, the immune cells processing the mRNA and the produced protein are targeted for destruction. The vaccine developed by Moderna is part of the Operation Warp Speed programmed to speed up vaccine production. It is currently recognized by the World Health Organization (WHO).

NON-REPLECATING VIRAL VECTOR VACCINE

AstraZeneca/University of Oxford

The University of Oxford has partnered with AstraZeneca, a British pharmaceutical company, to create AZD1222, a non-replicating chimpanzee viral vector vaccine that was formerly known as ChAdOx1. AZD1222 is now winning the clinical trials race and has been approved by the World Health Organization. It is also a part of the Operation Warp Speed effort. In pig models, preclinical experiments revealed a strong antibody response**.**

CanSino Biological inc./Beijing Institute of Biotechnology

CanSino's Ad5-nCoV vaccine is a non-replicating viral vector vaccine that inserts the SARS-CoV-2 gene into the human body using the Ad5 adenovirus. CanSino has previously been involved in the development of an Ebola vaccine. The Ad5-nCoV vaccine had no adverse responses within 28 days of inoculation, according to data published in the journal Lancet from its Phase 1 trials. CanSino tested the effects of dose-escalation on 108 healthy persons in Wuhan between the ages of 18 and 60 who were randomly assigned to one of three dose groups (5 1010 virus particles, 1 1011 viral particles, or 1.5 1011 viral particles). The most prevalent side effects included pain at the injection site, fever, muscle aches, headaches, and exhaustion. These symptoms were encountered by ten people in Grade 3, with six of them in Grade 4. These symptoms were experienced by ten people at the Grade 3 level, six of whom were in the high dose group and accounted for 17% of the high dose group. Hyperglycemia, elevated total bilirubin, and 5 alanine aminotransferase levels were also recorded by few patients, although these were not judged clinically important.

COMMON SIDE EFFECT OF COVID-19 VACCINES

Reported side effects of COVID-19 vaccines have mostly been mild to moderate and have lasted no longer thana few days. Typical side effects include pain at the injection site, fever, fatigue, headache, muscle pain, chills and diarrhea.

DATA SUPPORTING EFFECTIVENESS (EFFECTIVE DATA OF VACCINES)

The EUA for a single booster dose of the Moderna vaccine for anyone aged 18 and up (administered as half of the dose of a primary series dose) and Pfizer-BioNTech, FDA's review of immune response data for COVID-19 vaccines supported usage in previously permitted populations for boosters.

The FDA compared the immune responses of 149 participants 18 years of age and older from the original clinical studies who received a booster dose at least six months after their second dose to the immune responses of 1,055 study participants after completing their two-dose series for **the Moderna COVID-19** Vaccine booster dose. The antibody response against the SARS-CoV-2 virus showed a booster response 29 days following a booster dose of the vaccination.

The FDA reviewed the immune response data from around 200 participants aged 18 to 55 who received a single booster dose of **the Pfizer-BioNTech** COVID-19 Vaccine**.**

CURRENT KNOWLEDGE ABOUT OMICRON

Researchers in Johannesburg and around the world are conducting studies to better understand many aspects of Omicron and will continue to share the findings of these studies as they become available.

Transmissibility

It is not yet clear whether Omicron is more transmissible (e.g., more easily spread from person to person) compared to other variants, including Delta. The number of people testing positive has increased in areas of South Africa affected by this polymorphism, although epidemiologic studies are being planned to assess if this is attributable to Omicron or other variables. [17].

Severity of disease

It's unclear whether Omicron-induced infections are more severe than those caused by other variations like Delta. According to preliminary data, hospitalization rates in South Africa are rising, however this could be due to an increase in the general number of persons becoming infected rather than a specific Omicron illness. At this time, there is no evidence that the symptoms associated with Omicron are distinct from those associated with other variations. Although determining the severity of the Omicron type will take days to weeks, the first cases of infection were among university students, who were younger and had a milder form of the disease. All COVID-19 variants, including the worldwide prevalent Delta variant, can cause serious illness or death, particularly in the most vulnerable individuals, hence prevention is always the best approach [17].

Effectiveness of vaccines

WHO is working with technical partners to see how this variance will affect existing countermeasures like vaccination? Vaccines, particularly those against Delta, the most common circulating type, are critical in reducing severe disease and death. Immunizations that are currently available are still effective in preventing serious illness and death.

Effectiveness of current tests

Commonly used PCR assays continue to identify infection, even infection with Omicron, as we've seen with earlier variations. Other diagnostics, such as rapid antigen detection tests, are being investigated to see if they have any influence.

Effectiveness of current treatments

Corticosteroids and IL6 receptor blockers will still help patients with severe COVID-19. Other treatments will be assessed to see if they are still effective in light of the Omicron variant's changes to the virus [17].

CONCLUSION

When compared to conventional vaccine development, Coronavirus illness 2019 vaccine development is moving quickly (within months) (taking several years). The expedited development, on the other hand, does not jeopardize non-clinical or clinical safety evaluations. SARS-CoV-2 vaccine licensure will contain all nonclinical and clinical data required for regular vaccine licensure. These vaccines' effectiveness and increased disease evaluations will also be evaluated in nonclinical animal models and clinical trials. Preliminary data from nonclinical efficacy, immunogenicity, and safety studies have been promising, and efficacy and safety data from clinical trials of the major vaccine candidates are all available today. It is critical that academics, industry, regulatory agencies, and other stakeholders collaborate to create safe and effective vaccinations to combat the pandemic. Vaccine candidates have recently been granted an Emergency Use Authorization. Furthermore, for Pfizer/BioNTech, Moderna mRNA vaccines, and Johnson & Johnson viral vector vaccine all are made by the US and Food drug administration and the AstraZeneca vaccines are made by the oxford university of United Kingdom. Sinopharm by China government have recently granted Emergency Use Authorization to vaccine candidates. and by Indian government COVISHEILD AND COVAXIN made by (Bharat biotech).

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