ejpmr, 2021,8(7), 300-304

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

COVID-19 VACCINES DEVELOPMENT – "RECENT DEVELOPMENT AND CHALLENGES"

***Noorush Shifa Nizami and Dr. Somnath De**

[1]Intern Clinosol Research, Doctor of Pharmacy (PHARM-D), Clinosol Research Private Limited, Ameerpet, Hyderabad, Telangana (500038), India. St Paul's College of Pharmacy, Turkayamjal.
[2]M.Pharm., Ph.D, Professor & HOD, Department of Pharmacology and Pharmacy Practice, Narasaraopeta Institute of Pharmaceutical Sciences, Narasaraopet - 522601, Guntur (dist.), Andhra Pradesh, India.

***Corresponding Author: Noorush Shifa Nizami**
Intern Clinosol Research, Doctor of Pharmacy (PHARM-D), Clinosol Research Private Limited, Ameerpet, Hyderabad, Telangana (500038), India. St Paul's College of pharmacy, Turkayamjal. **Email Id:** sarita.pgaikwad@gmail.com

Article Received on 13/05/2021 **Article Revised on 03/06/2021** **Article Accepted on 23/06/2021**

ABSTRACT

In December 2019 there was an information emerged about the "respiratory illness". Immune system is basically comprised of collection of various cells, different processes, and chemicals which constantly defends the body against invading pathogens, which includes viruses, bacteria and other toxins. Keeping the immune system healthy and strong year-round is the key to prevent infection and diseases. Due to the pandemic there was an increased medical risk all over the world which was mainly related to covid-19. Due to limited and decreased supply, few countries are planning to mainly maximize the immunity of the population thereby postponing the second dose of the vaccines and for the same reasons and new vaccine trials are being assessed, mix and match schedules which in turn administer different vaccine products to the same individual. Though vaccines have not cleared all the phases of clinical trials vaccines may also cause the adverse events which may be temporary or maybe life threatening also. The main objectives of vaccination includes reduction of pressure on health care system, reduction of overall covid-19 mortality and severity, reopening of society and disease elimination. Therefore vaccines can be sustainable, continual and feasible solution to the covid-19 pandemic.

KEYWORDS: COVID-19, Vaccines, Disease elimination, severity, clinical trials.

INTRODUCTION

December 2019 the information emerged about the mysterious respiratory illness in Wuhan, a city in Hubei China and then six months later, in the context of greater than ten million cases, the COVID-19 pandemic has now become the worst public health crisis of the last century (Docea AO, et al.,2020). Then in December 2020, an unprecedented vaccination campaign has been started against COVID-19 b in the EU and globally (European Centre for Disease Prevention and Control, 2020). Member States have identified the priority groups for vaccination among those at an increased medical risk related to severe COVID19 and those including high exposure to infection. The systems were kept in place to facilitate orderly roll out of vaccine in many countries and however, the challenges in the production of vaccine, supply and logistics have caused delays in the deployment of vaccines among target groups.

Current Scenario

The current scenario is dynamic and there are still few number of important uncertainties. Due to the limited supply, some countries are adopting the strategies to mainly to maximise the immunity of the population by postponing the second dose of the vaccines and for the same reason, the new vaccine trials are being assessed, mix and match schedules which in turn administer different vaccine products to the same individual. In coming months, the new vaccine products, which are built on the different technological platforms, will be anticipated to reach the EU market and supply is expected in order to increase substantially (V Shah AS, et al.,2021).

Vaccination strategies by objectives

1. Reduction of pressure on the healthcare system

Health and social crisis has been developed worldwide by SARS-CoV-2 this is primarily because of large number of deaths as well as the heavy pressure on the HCP as well as healthcare systems because of so many individuals being hospitalised and are in need of intensive care. Surveillance data have reported that nearly 90 percent of deaths and 80 percent of hospitalisations have occurred in the older population and persons with underlying diseased conditions such as hypertension, diabetes, thyroid disorders as well as other diseased conditions.

2. Reduction Of Overall Covid-19 Mortality And Severity

While prioritising the vaccination depending upon age alone is mostly efficient and simple, given the steep increase at the risk of the severity as well as death in the case of COVID-19. Although it is worth bearing in mind that few of the individuals are also at increased risk of serious disease due to the known underlying health conditions as well as co morbidities, including age. Therefore, with spread of more transmissible, and also possibly more and more aggressive SARS-CoV-2 variants of the concern, there is a greater risk that the absolute number of hospitalisations and deaths due to COVID-19 may get increase in the younger as well as healthier groups (Dagan N et al.,2021).

3. Re Opening Of Society

When the vaccine supply will be readily available then the goal of re-opening society by lifting non-pharmaceutical interventions will then become realistic. The vaccination strategies that are employed to achieve this goal will need to facilitate the substantial reduction and not only in COVID-19 mortality and hospitalisations, but also in overall morbidity which is caused by COVID-19. During this pandemic, millions of peoples have lost so many days of healthy life and work because of the disease and the numerous individuals will be affected by the long-term consequences of COVID-19.

4. Disease Elimination

A disease elimination goal is the important appealing, and also the most costly objective for any of the vaccination programme and COVID-19 is no exception. If at all this route is chosen, the clear elimination threshold should be well quantified and defined, as for the other diseases (e.g. measles, cervical cancer). In the COVID-19 vaccination elimination strategy, the main focus would then shift from the protection of most vulnerable groups to a targeting of the groups those that have the increased level of contact with others, including young generation as well as children. The strategy will be dependent on vaccines offering the high level of efficacy against onward transmission (Voysey M et al.,2021). The contribution of children in the spread of SARS-CoV-2 is still unclear and there are no vaccine products authorized for the people younger than 16 years of age. There are many uncertainties that are majorly concerning the duration of protection and the also the effectiveness of COVID-19 vaccine products against SARS-CoV-2 onward transmission, that are particularly given the new variants emerging and continuous escape mutations (Lavine JS et al.,2021).

Different Covid-19 Vaccines

All the vaccines that are currently authorized and recommended as COVID-19 vaccines are safe and effective and they in turn reduce the risk of severe illness and CDC does not recommend one vaccine over another (Bubar KM et al.,2021).

There are mainly three major approaches in order to design the vaccine. Their differences will usually lie between, whether they use a whole virus or bacterium, just the parts of the germ that will ultimately trigger the immune system, or the genetic material which will provide the instructions in order to make a specific protein and not the whole virus.

- **Inactivated vaccine**

The important and the foremost way to make the vaccine is to take the virus or bacteria that causes the disease and kill it by using the chemicals, heat or radiation or either inactivate heat or radiation. This approach mainly will use the technology which has been reported to work in people, this was the is the way through which flu and polio vaccines were made, therefore, it requires the special laboratory facilities to grow the virus/ bacterium safely and can have the relatively long production time, and it will likely require 2 or 3 doses usually to be administered for the complete effect.

- **Live-attenuated vaccine**

The live-attenuated vaccine will mainly use the living but it is the weakened version of a virus and also the one that's very similar. The (measles, mumps and rubella) MMR vaccine and also the "chickenpox" and "shingles" vaccine are the best examples of this type of vaccine. This approach mainly uses similar technology to inactivated therefore the vaccines like this may not be suitable for people with compromised immune systems.

- **Viral vector vaccine**

This is the another type of vaccine which uses the safe virus in order to deliver the specific sub-parts 'known as proteins' of the germ of interest due to which it could trigger the immune response without causing any other disease. To do this, the instructions for making the most particular parts which belongs to the pathogen of interest are ultimately have been inserted into the safe virus. The safe virus will then serve as the platform or the vector in order to deliver the protein in the body. The protein will ultimately trigger the immune response. The Ebola vaccine is the viral vector vaccine and this type of vaccine has to be/can be developed rapidly.

- **The subunit approach**

The subunit vaccine is one of the type of vaccine which will only use the most specific parts "the subunits" of the virus/ bacterium that the immune system will need to recognize. It will not contain whole microbe/ use the safe virus as the vector. The subunits can be either proteins or it could be sugars. Mostly the vaccines on the childhood schedule are known as the subunit vaccines which are developed in order to protect people from the diseases known as whooping cough, diphtheria, tetanus and meningococcal meningitis.

- **The genetic approach (nucleic acid vaccine)**

Unlike the other the vaccine approaches that will use either the weakened/ the dead whole microbe or parts,

the nucleic acid vaccine will just use the section of the genetic material which provides the main instructions for the specific proteins not the whole microbe. Basically, DNA and RNA are the instructions which are being used by our cells to make the proteins. Inside the cells, DNA will be the first turned into the messenger RNA, which then will be used as the blueprint to make the specific proteins.

The nucleic acid vaccine will be delivering the specific set of instructions to the body's cells, either in the form of DNA or may be mRNA, for them in order to make a specific type of protein that we want our immune system to recognize and then respond to it.

Therefore, the nucleic acid approach is the new way of developing the vaccines. Before the COVID-19 pandemic, no one had yet been gone through full approval process for use in human beings, though some DNA vaccines, which also includes particular cancers, were undergoing the human trials. Because of COVID-19 pandemic, the research in this area has progressed very fast and due to which some mRNA vaccines for COVID-19 are getting the emergency use authorization, which also means that they can now administered to the people beyond using them only in clinical trials. However covid-19 vaccines will cause the side effects also which includes, fatigue, fever, headache, chills, body aches, nausea, diarrhea, pain/irritation at the site of injection.

1. *Pfizer-BioNTech* (people above 16 years can get this vaccine with 2 shots which can be given in 3 weeks (21 days) apart).
2. *Moderna* (people above 18 years can get this vaccine with 2 shots which can be given in 4 weeks (28 days) apart).
3. *Johnson & Johnson's Janssen* (people above 18 years can get this vaccine with only 1 shot).

Vaccines that are in phase 3 clinical trials as of February 27, 2021 with large scale phase 3 clinical trials are still in progress or which are being planned for two covid-19 vaccines in US are (Calina D et al.,2020).

1. *AstraZeneca Covid-19 vaccine*
2. *Novavax Covid-19 vaccine*

Covaxin* vs *Covishield

	COVAXIN	***COVISHIELD***
DEVELOPER	Covaxin has been developed by Hyderabad based Bharat Biotech International Ltd in association with ICMR and NIV (Indian council of Medical Research and National institute of virology)	It was developed by Oxford- Astrazeneca and is being manufactured by SII (Serum Institute of India)
TYPE OF VACCINE	Covaxin is inactivated vaccine which was prepared on tested and tried platform of dead viruses. The vaccine was developed with Whole-Virion Inactivated Vero Cell Derived technology which contains an inactivated viruses which will not infect the person but it can teach the immune system to prepare a defence mechanism against the active virus.	Covishield is prepared using the viral vector platform which is totally a different technology. A chimpanzee adenovirus (ChAdOx1) was modified to enable it to carry the Covid-19 spike protein into the human cells , this cold virus is basically incapable of infecting the receiver but it can teach the immune system to prepare against such viruses and the exact technology was used to prepare the vaccines for viruses like Ebola.
DOSES	Follows two-dose regimen, administered 28 days apart. Has been given to people aged 12 years and above. There is no assurance if the vaccine can be given to children and pregnant women.	Follows two-dose regimen, administered 28 days apart. Has been given to people aged above 18 years and above and there is no assurance if the vaccine can be given to children and pregnant women.
STORAGE	Can be stored at 2-8 degrees centigrade (house hold refrigerator temperature)	Can be stored at 2-8 degrees centigrade (house hold refrigerator temperature)
EFFICACY	Have shown more satisfactory results ever since the inoculation have started. Effectiveness is nearly 81% according to interim 3rd phase trial results	Have shown more satisfactory results ever since the inoculation have started. Effectiveness is nearly 90% according to interim 3rd phase trial results
Approvals	Has been granted a restricted-use authorization in the clinical trial mode	Has been allowed for restricted use in emergency situations

Therapeutic Effect

Basically the SARS-CoV-2 virus is studded with the proteins that it enters human cells, these spike proteins make a tempting target for the potential vaccines and their treatments. The vaccine uses messenger RNA as well as the genetic material that our cells read to make

proteins. The molecule known as mRNA for short is the fragile molecule and it would be chopped to pieces by the body's natural enzymes if it were injected directly into the body. To protect the vaccine, Pfizer and BioNTech wrap mRNA in the oily bubbles which are in turn made up of the lipid nano-particles. After infusion/injection, the vaccine particles starts to bump into cells and fuse to them, thereby releasing the mRNA. The cell's molecules starts to read its sequence and build spike proteins and the mRNA from vaccine is ultimately destroyed by the cell, by leaving no permanent trace (Khuroo MS et al.,2020). It will then spot the intruder after spotting it makes the antibodies the antibodies can latch onto the coronavirus spikes, thereby mark the virus for destruction and prevent the infection by blocking spikes from attaching to the other cells. The antigen presenting cells can also activate the other type of immune cell called a killer T cell to seek out/ destroy any coronavirus infected cell that will then display the spike protein fragments on their surface. It is possible that within the months after vaccination, the number of antibodies as well as killer T cells will drop. But our immune system also will contain the special cells called memory T cells and memory B cells that might retain information about the coronavirus for years or even decades.

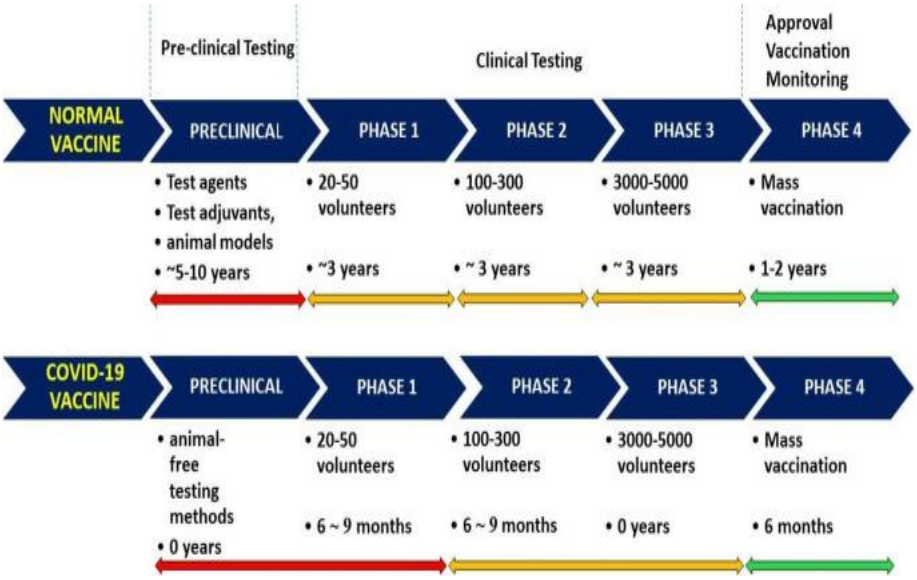

Figure 1: (A comparative scheme regarding the development of normal vaccines versus potential COVID-19 vaccines).

There are several studies in the development of a COVID-19 vaccine are in different stages of the development and some of the methods use messenger RNA, others that use DNA, which is specific and then translated and then the specific immunogenic proteins are produced. Wherein the basic research which determines what type of antigens could cause a neutralizing immune response against the virus, two very important elements should be used in the consideration of the development of a vaccine. These are known as the safety studies and efficacy studies which includes the safety and efficacy of the vaccines. During the development of the vaccine, it is very important to consider standard of the 3R's, i.e. Replacement, Reduction, and Refinement. In case of the standard vaccines, the fundamental properties are being tested pre-clinically (i.e. in vitro and in vivo) and subsequently in the human clinical trials, during so many years of research and in vivo vaccine testing is time-consuming process and most often, tests fail when the pathogens which are being tested are not specific to humans.

During previous SARS epidemic, it was ended, and we have had now the vaccine that is approved for the human use, all the steps of trial could most probably be skipped safely, and it is supported by the biological similarity of coronavirus is large enough. Therefore, if a SARS or MERS vaccine already existed, it could be very easily had been adapted for SARS-CoV-2 without any complex testing, as a consequence, it is mostly desirable for the development of the appropriate technologies that may respond swiftly to control the current COVID-19 pandemic (Bliss CM et al.,2018).

CONCLUSION

Vaccines are being considered as the critical tool in battle against the COVID-19 & there are the understandable public health as well as the life saving well-being of using the implements we already have. We should not put off getting vaccinated because of our thinking about the new variants and we should proceed with vaccination process as soon as possible even if vaccines be less effective against few of the COVID-19 virus variants. We have to use tools that we have in hand even when we continue to improve that tools. We are safe if everyone is safe. It is of dominant importance in order to define the clear and the measurable goals for the vaccination process against COVID-19 pandemic and to adapt the strategies according to the situation. During the times of the extreme unpredictability and high

expectation, it is essential and very important to clarify the steps that are required to reach final objective, but not resist the need to adapt to the unpredicted changes. As the part of pharmacovigilance and its postmarketing studies monitoring the vaccine safety as well as the effectiveness and collisions are of particular importance in providing the benefits of vaccination for all the target groups and each of the vaccination goals which has been outlined may require the most important factors which are culturally adapted as well as the contextual implications must be considered. The goals of the vaccination could be considered as the "sequential milestones" on behalf of long journey that will ultimately lead to the sustainable, continual and feasible solution to the COVID-19 pandemic.

REFERENCES

1. Docea AO, Tsatsakis A, Albulescu D, Cristea O, Zlatian O, Vinceti M, Moschos SA, Tsoukalas D, Goumenou M, Drakoulis N, Dumanov JM, Tutelyan VA, Onischenko GG, Aschner M, Spandidos DA, Calina D. A new threat from an old enemy: re-emergence of coronavirus. Int J Mol Med, 2020; 45(6): 1631–1643. Accessed on May 4, 2021.
2. European Centre for Disease Prevention and Control. COVID-19 vaccination and prioritisation strategies in the EU/EEA. Stockholm: 22 December 2020. Accessed on May 4, 2021.
3. V Shah AS, Gribben C, Bishop J, Hanlon P, Caldwell D, Wood R, et al. Effect of vaccination on transmission of COVID-19: an observational study in healthcare workers and their households 2021. Accessed on May 4, 2021.
4. Dagan N, Barda N, Kepten E, Miron O, Perchik S, Katz MA, et al. BNT162b2 mRNA COVID-19 Vaccine in a Nationwide Mass Vaccination Setting. N Engl J Med. 24 February 2021. Accessed on May 4, 2021.
5. Voysey M, Costa Clemens SA, Madhi SA, Weckx LY, Folegatti PM, Aley PK, et al. Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: a pooled analysis of four randomised trials. Lancet, 2021 Mar 6; 397(10277): 881-91. Accessed on May 4, 2021.
6. Lavine JS, Bjornstad ON, Antia R. Immunological characteristics govern the transition of COVID-19 to endemicity. Science, 2021 Feb 12; 371(6530): 741-5. Accessed on May 4, 2021.
7. Bubar KM, Reinholt K, Kissler SM, Lipsitch M, Cobey S, Grad YH, et al. Model-informed COVID-19 vaccine prioritization strategies by age and serostatus. Science, 2021 Feb 26; 371(6532): 916-21. Accessed on May 4, 2021.
8. Calina D, Hartung T, Docea AO, et al. COVID-19 vaccines: ethical framework concerning human challenge studies. DARU J Pharm Sci., 2020; 1–6. 10.1007/s40199-020-00371-8. Accessed on May 4, 2021.
9. Khuroo MS, Khuroo M, Khuroo MS, Sofi AA, Khuroo NS. COVID-19 Vaccines: A Race Against Time in the Middle of Death and Devastation! J Clin Exp Hepatol. 2020. Accessed on May 4, 2021.
10. Bliss CM, Bowyer G, Anagnostou NA, Havelock T, Snudden CM, Davies H, de Cassan SC, Grobbelaar A, Lawrie AM, Venkatraman N, Poulton ID, Roberts R, Mange PB, Choudhary P, Faust SN, Colloca S, Gilbert SC, Nicosia A, Hill AVS, Ewer KJ. Assessment of novel vaccination regimens using viral vectored liver stage malaria vaccines encoding ME-TRAP. Sci Rep, 2018; 8(1): 3390. Accessed on May 4, 2021.