

Covid-19 Vaccines and their Interchangeability Could be Effective in Developing Countries Like India to Generate Stronger Adaptive Immune Response in Large Population

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ABSTRACT

Vaccine considered as a boon for every individual across the world in the time of pandemic situation. India has developed its own vaccine which shows promising results. Receiving vaccine does not mean that we are completely immune to the disease. Covishield shows some rare but adverse side effects of blood clots in those people having thrombocytopenia. Covaxin has not recorded any such cases as it is of inactivated type. But, the manufacturers of the vaccine have not established the longevity of protection against COVID-19. Unavailability of vaccines in India could pose a serious impact on the lives of the people. Government of India and Medical authorities should take clinical trials and make decision on interchangeability of vaccines as soon as possible.

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Introduction

A vaccine is a biological compound which provides adaptive immunity to a particular disease with long term effects. Vaccine contains same pathogen that causes disease, administered into a body into weak or killed form so that pathogen may not infect our body. It will only boost our immune system to produce antibodies for particular diseases. Vaccination is the most effective method of preventing infectious diseases. Vaccines contain different components to keep the vaccine safe and effective. Each vaccine component has its specific function and tested in manufacturing process. The components of vaccine comprise of preservatives, antigens, diluent, surfactants, adjuvants etc. Antigen can be used as a pathogen's active part like protein, sugar or can be a whole pathogen. The aluminium salts are used as an adjuvant in tiny amounts for improving immune response to vaccines.

Once the vaccines are developed it undergoes preclinical trials, it is first tested on animals to evaluate its safety for human trials. In human trials, vaccine is given to the peoples in 3 phases. A lot of people believe that once get the COVID-19, your immune system immediately becomes strong enough to defeat the disease if it comes again regardless of when reinfection happens. Some are even going out of their way to catch the disease intentionally with the hope of building immunity. There are two types of immunity that can happen within our body once we get an infection- Humoral and Cell mediated immunity. In humoral immunity our B-cells produce antibodies against the virus and then secrete these antibodies into the bloodstream. However, the antibodies released into the bloodstream are not long-lasting. Antibodies are basically

proteins made of amino acids, and proteins that are released out of the cell into bloodstream are unstable. In other words, they are subjected to wear and tear. Through time, their structure changes dramatically and they eventually lost their function, which in this case is identifying the coronavirus and neutralizing it. As time passes, the number of antibodies in the bloodstream begins to decline as well. One study found that antibodies in COVID-19 survivors can still be detected up to six months after recovery. This means after six months, covid survivors are likely to get reinfected. Our B-cells then go to the extra mile and form a memory against the pathogen, which allows them to produce fresh antibodies quickly as soon as they encounter the virus again. Fresh antibodies are stronger than those that have been circulating in your blood stream for a while. This is because their structure is still intact, and hence can perform their function properly. Memory B cells can survive in the body for decades, offering a long-term protection against the same infection. A number of studies showed that even mild covid infections can trigger the formation of memory B cells, however it remains unclear how long they can last in the body. With time, memory B cells will upgrade their genetic instructions to redefine the antibodies. In other words, they continue to create different versions of the antibodies and eventually choose the most potent version that can neutralize the virus more efficiently [1].(Oliviero et al., 2020). Although many COVID-19 survivors have antibodies against the virus, it's not yet well-known whether people with such immunity are completely protected from reinfection or whether they would just become less severely ill if exposed to the virus again [2].

The second type of immunity is called cellular immunity. This is where our immune cells except antibodies directly attack the virus. T-cells would recognize and kill the virus while another type of

cells called phagocytes would engulf the remains of the virus and remove it from the site of infection. This type of immune response is very powerful and fast-acting. And just like memory B cells, we also have memory T cells, which also remembers the pathogen and act quickly to get rid of it [3]. Recent studies revealed that COVID-19 patients including mild and asymptomatic shows a sign of cellular immunity for as long as six months [4]. However, these findings are questionable given that they tested a small group of hundred patients. Whether this immunity is helpful to the patient or not depends largely on a number of factors such as preexisting conditions, genetics, age and sex of the person. Some people do not develop full immunity against reinfection because their immune system is weaker than that of younger people. It may not have enough B cells to produce sufficient antibodies to prevent the infection. Similarly, people with preexisting conditions might not benefit greatly from such immunity if their preexisting illness compromised their immune system. Therefore, it remains important to be careful before exposing yourself or loved ones to the virus with the hope of building immunity against the disease [5].

On the other hand, the vaccine is intended to help the body develop long-term immunity against reinfection, which can last for decades. It does so by provoking the body to generate long-lived memory B cell and memory T cell. Generally, when you get infected, your immune system takes time to respond. The virus uses this time for its own advantage to destroy as many tissues as possible while also making more copies of itself. The vaccine is intended to help our body to build this immunity before infection happens, thus saving the time it takes to respond to viral attacks. Effective vaccines are designed to induce sterilizing immunity, which is a type of immunity that completely blocks the infection from happening. If the newly developed COVID-19 vaccines elicit sterilizing immunity, it would be the best-case scenario to the pandemic and resume normal life.

Present Scenario of India's on COVID-19

According to WHO, from 3 January 2020 to 5:03pm CEST, 28 May 2021, there have been 27,555,457 confirmed cases of COVID-19 with 318,895 deaths. A total of 200,494,991 doses of vaccine have been administered till 24th of May 2021 [6].

In the current year 2021, the covid cases are on its peak in the month of April and May 2021. Maximum number of deaths recorded due to shortage of oxygen as hospitals in different cities ran out of beds. Covid patients get no choice rather than treating the disease at home.

As death cases started increasing, people started black marketing different drugs like Remdesivir and Tocilizumab. The effectiveness of these two drugs was debated across the world but in India it is given preference and being prescribed by doctors across the country. As cases were increasing day by day, the huge crowd of people were seen at the Covid testing centres. Private testing labs have given the authority to conduct a test at reasonable price according to government guidelines. At government hospitals, free covid test were conducted including Rapid Antigen and RT-PCR (Reverse Transcriptase Polymerase Chain Reaction) test. Peoples also have to wait for several hours to get tested for Covid at government hospitals and private labs. Rapid antigen tests result has been given to the patients with in half an hour while report for RT-PCR test is given after 48- 72 hours due to high work load. The second wave of covid has hit India hard. The members of India task force had taken some urgent steps to reduce the cases of covid-19. Vaccination is only the key to combat the spread of

Covid-19. Government targeted to administer the five million doses per day especially for the individuals of age above than 45 years. According to the government data 29.6% of this age group have received one or both doses of vaccine till 11 April 2021. At this moment, government deploys the use of two vaccine: Covishield and Covaxin (Press Information Bureau,2021).

Covaxin and Covishield

The Covaxin is the India's first vaccine developed by Indian Council of Medical Research (ICMR) in partnership with Bharat Biotech International Limited (BBIL) shown 81% efficacy in phase 3 trial against SARs-CoV-2. The vaccine is developed by using entire virion inactivated vero cell. Inactivated vaccines do not replicate and thus there are less chances of causing pathological effects. The vaccine contains dead virus and therefore incapable to cause infection but still able to generate immune response in the body [7].

Covishield is a recombinant chimpanzee adenovirus vector (ChAdOx1) derived vaccine which encodes the SARs-CoV-2 spike glycoprotein. It stimulates an immune response when part of corona virus is expressed in the human body. Oxford AstraZeneca vaccine is locally manufactured in India as Covishield by Serum Institute of India. The Covishield regimen consist of two doses with same content of viral particles. The vaccine consists following excipients including: L-histidine, L-Histidine monohydrate, Magnesium chloride hexahydrate, polysorbate 80, Ethanol, sucrose, sodium chloride and EDTA. Those people who have previous disease history or current (including Hypertension, Diabetes mellitus, Asthma and cardiovascular diseases) can take vaccine only when having a risk benefit assessment based on clinical judgement by the physician. The Serum Institute of India gave some contraindications regarding vaccine, people having hypersensitivity to the active substance or excipients listed in the vaccine. Their clinical trials showed persons after two doses of vaccines developed antibodies in almost all recipients. However, CDC (Centre for Disease Control), USA does not recommend any antibody test to check the immunity for SARs-CoV-2 after vaccination [8]. The Indian government has recommended the time interval should be 12-16 weeks between first and second dose [9]. However, the immunity provided by vaccine for long term has not been established yet.

Pfizer and AstraZeneca vaccines are found highly effective against India COVID-19 variant. The data emphasize the importance of getting both doses of the vaccine. The analysis found the Pfizer vaccine was 88% effective against symptomatic disease of Indian variant B.1.617 compared with 93% effectiveness against the Kent variant. Effectiveness results were measured two weeks after a second dose. The AstraZeneca jab was 60% effective compared with 66% effectiveness against the Kent variant over the same period. Data also shows it takes more time to reach maximum effectiveness with the AstraZeneca vaccine. The studies shows that effectiveness after one dose of vaccine was remarkably lower with the Indian variant. One dose was 33.5% effective against the India sub-variant B.1.617.2 compared to 51.1% effectiveness against the UK variant B.1.1.7. The results were comparable for both vaccines. Researchers said that the protection offered should be even more effective against hospital admissions and deaths. The analysis is based on a study carried out on people from all age group. The study covered the period when the India variant emerged. Total 1054 people participated in the study. These were confirmed as having the variant through genomic sequencing. India has experienced a surge in COVID-19 cases since late March 2021 reaching over 400,000 cases and 4000 deaths reported each

day in early May 2021. This has resulted in hospital services becoming overwhelmed in addition to scarcity in oxygen supplies. While only a small proportion of samples have been sequenced. B.1.617 lineages have dominated the recorded cases. B.1.617.2 was first detected in India in December 2020 and became the most commonly reported variant across the country. The variant had been detected in more than 40 countries across 6 continents [10].

Fusion of Vaccines

The National Advisory Committee on Immunization (NACI) recommended the Public Health Agency of Canada to interchange the doses of authorized COVID-19 vaccines. It means people can receive one vaccine product as first dose and different vaccine product for second dose to complete two dose series. Interchangeability of vaccines is not a new concept. Similar vaccines are used when supply is limited to complete the vaccine series for Influenza, Hepatitis A and others. A condition called Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT) has been associated with AstraZeneca, Covishield and other viral vector vaccines. Due to this minor but serious effect, several European countries start giving second dose of mRNA vaccine to those who have received first dose of viral vector vaccine [11]. Recent studies gave evidence on the immune response produced by the mixed COVID-19 vaccine. The study conducted on the participants at Val d'Hebron University at Barcelona, Spain showed Pfizer BioNTech boost the immunity of the AstraZeneca dosed peoples reported by Magdalena Campins, participants had produced much higher level of antibodies than before. The mixing of vaccines showed promising results than earlier trials with same dose of vaccine [12].

According to me, in developing countries like India would also look on it to recommend the interchangeability of vaccines after making trials as soon as possible. Like other countries India have now 2-3 authorized vaccines. From the recent 2-3 months there have been shortage of vaccines especially Covishield. On the other hand, Government has also increased the time duration between first and second dose of Covishield which is about 12-14 weeks. So, in that case people will easily go for Covaxin as a second dose. Indian Government should make trials on this, so there will be a possible chance of generating long lasting immunity in the large population. The vaccine having mRNA as a virus part evokes stronger adaptive immune response and teaches body cells to identify and encounter protein encode by the mRNA. Whereas inactivated vaccines are quite slow in generating immune response as it contains the dead particles of virus or complete pathogen which take time by the body to identify the dead particles of pathogens and to generate immune response. So, combination of Covishield and Covaxin would show promising results in generating stronger and prolong cellular and humoral immune response [13].

Conclusion

The different vaccines show different efficacy after administration into the body. The efficacy of vaccine also varies from person to person as every individual has its own immunity which is affected by their lifestyle. The shortage of vaccines in India is creating a problem and helps in increasing the infection and mortality rate. Fusion of two vaccine doses could help in building the stronger immune response as there are many corona virus variants. Getting the same doses of single vaccine could provide immunity against virus but how long it has not been established yet. So, its better to take vaccine of two different types which definitely induce our body immune response and may also provide long lasting

immunity as evident by studies [14].

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