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Perspective

A Virus Taking Shape of a Nuclear Bomb - A New Vaccine to Defuse the SARS-CoV-2 Virus

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SARS-CoV-2 infection fell on earth just like a nuclear bomb with devastating effects on human life. SARS-CoV-2 affects respiratory system profoundly, causing huge death toll to even in the affluent countries like United States and many others. Also, the developing countries including India having a population of more than a billion were not spared and huge mortality and morbidity resulted. Again, control of virus through Public Health Measures like wearing of masks, sanitization and social distancing were not full proof to control the disease. Even the asymptomatic patients carry a viral load and they are the major cause of spread of the disease. All these factors pose a great challenge to the scientists to find measures to control SARS-CoV-2 effectively. So comes the thought of vaccine against the virus.

SARS-CoV-2 caused explosion of infection throughout the world. Our aim is safe and effective vaccines that can be widely deployed everywhere in the world which will also provide herd immunity and will control viral spread.

In 2020 January the first sequencing of SARS-CoV-2 became public. Since then scientists in different parts of world started working on finding out effective vaccines from mRNA, Protein, Viral vectors and also other types of Covid vaccine m-RNA. Efficacy trials of vaccines continued. Following extensive and rigorous efficacy trials two vaccines have gained Emergency Use Authorisations (EUA) from Food and Drug Administration (FDA), U.S.A.

95% vaccine efficacy was shown by m-RNA in lipid nanoparticles (LNPs), BNT162b2 from Pfizer and BioNTech and they received EUA.

The trial results establishing the efficacy of a second mRNA-LNP vaccine, mRNA-1273 from Moderna was published in various journals. Efficacy (COVE) trial for mRNA-1273 Corona Virus was done randomisely to volunteers with either vaccine or placebo. Total 30,420 volunteers were included in trial, half of them received vaccine and other half placebo (15,210 in each group). In this trial symptomatic Covid-19 was seen in 185 volunteers in the placebo group and only 11 in the mRNA-1273 group, for a vaccine efficacy of 94.1% (95% confidence interval, 89.3 to 96.8). 86.4% was the efficacy for persons above 65 years. But for 18 to less than 65 years of age, the efficacy was 95.6%. The final observation is that in both Moderna vaccine and the Pfizer-BioNTech vaccine the protection starts 10 days after the first dose but maximum protection comes after the second dose.

The mRNA-1273 vaccine was studied for its safety profile also. The frequency of unsolicited adverse events and severe adverse events during 28 days after injection was similar in both the vaccine and placebo groups. This is a report of median 2-month follow-up study. This indicates that there is no safety concern about the vaccine. After second dose of vaccine 88.6% vaccine showed Solicited adverse events at the injection site. This is much lower with placebo. mRNA-1273 vaccine was studied earlier on older persons with confirmed safety and immunogenicity.

Earlier studies on SARS and Middle East Respiratory Syndrome (MERS) there was a concern whether Covid-19 vaccine will increase Vaccine-Associated Enhanced Disease (VAED). In the earlier SARS and MERS preclinical studies, VAED occurred with low neutralizing antibodies. Thus, it will be important for the FDA and the Centers for Disease Control and Prevention to continue to monitor clinical trials for safety after issuing an EUA, including assessment of VAED risk.

In the placebo group of COVE trial 30 participants developed severe Covid-19. So, it is clear that 100% protection against severe Covid-19 disease can be obtained with the mRNA-1273 vaccine and without any VAED. It was observed that VAED occurred with low neutralizing antibodies in the earlier SARS and MERS preclinical studies.

Thus, is necessary to continue to monitor clinical trials even after issuing an EUA by the FDA and the Centers for Disease Control and Prevention, this is for the safety of the vaccine. Assessment of VAED risk should also be noted.

Now the question arises how Covid-19 vaccines mitigate the SARS-CoV-2 pandemic.

First, if the vaccine induces some protective immune response to SARS-CoV-2 then what are the nature and the duration of such immune response? Studies in vaccinated monkeys revealed that primary mode of protection are SARS-CoV-2 neutralizing antibodies. It was also observed that protection is augmented by CD8 T-cell responses. Now the question arises how long these neutralizing antibodies will last? In answer it can be said that duration of neutralizing antibodies is not fully known but in Phase I trial of mRNA-1273 neutralizing antibodies were present three months after second dose of vaccine.

The medical community of the world had lost control of the Covid-19 pandemic because of the respiratory spread of SARS-CoV-2 and to ineffective public health measures which include wearing masks and maintaining social distancing and sanitation. Persons infected with SARS-CoV-2 are frequently asymptomatic, but they have high respiratory viral loads and they are the major suppliers of viral spread. These factors have led to the explosion of Covid-19 hospitalizations and deaths, with Covid-19 now is a major cause of death in the United States and many other parts of the world like India. Our only hope is safe and effective vaccines that can be widely deployed to provide herd immunity that can control viral spread.

Since the publication of the genome sequence of SARS-CoV-2, on January 11th, 2020, an endeavor of unprecedented speed and magnitude set out to develop a vaccine against the disease.

The scientific community has been working towards the rapid development of mRNA, protein, viral vector and other types of Covid-19 vaccines. Since then, there has been completion of two vaccine efficacy trials and leading to that two vaccines had received Emergency Use Authorization (EUA) from the Food and Drug Administration (FDA). The safety profile Solicited adverse events at the injection site occurred more frequently with the vaccine than with placebo, occurring in 88.6% of vaccines after the second dose. The safety and immunogenicity of the mRNA-1273 vaccine in older adults had been previously reported.

One of the major concerns regarding Covid-19 vaccines that have emerged from studies of the earlier SARS and Middle East Respiratory Syndrome (MERS) outbreaks is the possibility that a Covid-19 vaccine could enhance disease, a phenomenon called Vaccine-Associated Enhanced Disease (VAED). Now the question arises. First, what are the nature and the duration of the protective immune response to SARS-CoV-2? Neutralizing antibodies are the primary mode of protection in SARS-CoV-2 vaccine as evidenced in vaccinated monkeys. The effectivity is enhanced with CD8 T-cell responses. The longevity of such antibodies are not yet fully known. Follow-up studies in the phase 1 mRNA-1273 trial revealed that such antibodies persisted even 3 months after the second dose of vaccine. Secondly, in persons receiving vaccine reactogenicity was more. But people did not believed that minor symptoms may be due to Covid-19. So, they do not report for trial. Thirdly, what quantity of virus escape from protective immune responses of the vaccine need to be studied. In this area long-term follow-up is necessary so that rare safety measures can be developed if needed. Finally, to control the pandemic efficiently asymptomatic

SARS-CoV-2 infection also need to be controlled by the vaccine. But in mRNA-1273 trial this area was not covered. May be this will be considered in their ongoing studies.

Usually, scientific studies to establish the efficacy and safety of vaccine requires a prolonged study periods over years. mRNA-1273 Covid-19 and the BNT162b2 Covid-19 vaccines were developed and effectively tested in less than a year. Both the vaccines showed near identical 94% to 95% vaccine efficacies. To develop a vaccine in such a short time with a reasonable efficacy and safety may be attributed as a great scientific and medical triumph. Scientists working in medical domain were working on various vaccines against various infection worldwide like HIV, influenza, respiratory syncytial virus, and Zika for last few decades and hence the technology for vaccine preparation was already established. Improvement in vaccine technology and clinical trials consortia led to the rapid discovery of effective Covid-19 vaccine. Covid-19 vaccines have significantly controlled the pandemic at present but any virus may change itself by mutation. So, vaccines may need to be changed accordingly. If such outbreaks occurs m-RNA technology has the potential to change vaccine design.

Vaccine research on Covid-19 pandemic shows hope for control of future attacks. Covid-19 created a devastating effect on many countries of the world and possibly no country were spared. Allowance of use of such protective vaccines in various countries ushers hope for suffering people. The countries should take proper measure so that the Covid-19 vaccines reach the people at risk at the earliest along with people in general.

Coverage of maximum number of people with vaccine is the key issue to control this nuclear bomb like infection [1-5].

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