

EDITORIAL

The British variant of the new coronavirus-19 (Sars-Cov-2) should not create a vaccine problem

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Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a highly contagious virus that infects humans and a number of animal species causing coronavirus disease-19 (COVID-19), a respiratory distress syndrome which has provoked a global pandemic and a serious health crisis in most countries across our planet. COVID-19 inflammation is mediated by interleukin (IL)-1 and is a disease that can cause symptoms such as fever, cough, lung inflammation, thrombosis, stroke, renal failure and headache, to name a few. Strategies that inhibit IL-1 are certainly helpful in COVID-19 and can represent one of the therapeutic options. However, to date, COVID-19 therapy has been scarce and, in many cases, ineffective, since there are no specific drugs other than vaccine that can solve this serious health problem. Messenger RNA (mRNA) vaccines, which are the newest approach, are already available and will certainly meet the many expectations of the population. mRNA vaccines, coated with protected soft fatty lipids, use genetic mRNA (plus various inactive excipients) to make a piece of the coronavirus spike protein, which will instruct the immune system to produce specific antibodies. The soft fatty lipids allow the entry of mRNA into cells where it is absorbed into the cytoplasm and initiates the synthesis of the spike protein. In addition, vaccination also activates T cells that help the immune system respond to further exposure to the coronavirus. mRNA induces the synthesis of antigens of SARS-CoV-2 virus which stimulates the antibody response of the vaccinated person with the production of neutralizing antibodies. The new variant of the coronavirus-19 has been detected in the UK where, at present, the government has imposed a lockdown with restrictions on international movements. The virus variant had already infected 1/4 of the total cases and in December 2020, it reached 2/3 of those infected in the UK. It has been noted that the spreading rate of the British variant could be greater than 70% of cases compared to the normal SARS-CoV-2 virus, with an R index growth of 0.4. Recent studies suggest

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that coronavirus-19 variation occurs at the N501Y level of the spike protein and involves 23 separate mutations on the spike, 17 of which are linked to the virus proteins, thus giving specific characteristics to the virus. In general, coronaviruses undergo many mutations that are often not decisive for their biological behavior and do not significantly alter the structure and the components of the virus. This phenomenon also occurs in SARS-CoV-2. It is highly probable that the variants recently described in the UK will not hinder vaccine-induced immunity. In fact, the variant will not neutralise the vaccine, although it may possibly make it a little less effective. It is therefore pertinent to think that the vaccine will work also against the SARS-CoV-2 variant. In today's pandemic, the D614G mutation of the amino acid of coronavirus-19, which emerged in Europe in February 2020, is the most frequent form and causes high viral growth. The previously infrequent D614G mutation is now globally dominant. This variant, which is being tested in many international laboratories, is rapidly spreading across the continents and a series of vaccinated subjects are being tested to see whether their antibodies can neutralize the new variant of SARS-CoV-2. This variant has a very high viral growth and is less detectable with the RT-PCR technique in the laboratory. It has been reported that the British variant that increases viral load does not cause more severe effects in the respiratory tract and lung disease, therefore, it is certain that the variant is growing rapidly and must be kept under control; for this reason, laboratory data is awaited impatiently. The study on the many variants that coronavirus-19 presents is very interesting and complete and clearer data on this topic will be available in the near future. In addition, it is still unclear whether the different variants discovered in many countries, including Africa, share the same spike protein mutation and therefore, this is another study to elaborate on. In order to be certain and to not have unexpected surprises, we need to reduce the spread and the transmission speed of viral variants that could appear around the world, creating new pandemics. For this reason, the scientific community is on the alert since laboratory tests on serum antibodies from COVID-19 survivors have been reported to be less effective in attacking the variant. In light of the above, the scientific community must be on the alert as larger variants of the spike protein could escape vaccine-induced antibodies, which for now are of great help to the community and can save millions of lives. In depth study of spike protein mutations will help to better understand how to combat coronavirus-19 and its variants.

In December 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged for the first time and spread globally, causing an unprecedented severe viral pandemic (1). SARS-CoV-2 is a highly infectious virus that remains active even at temperatures below 0°C, as has been seen recently. The global infection has affected over 40 million people and over a million have died. SARS-CoV-2 can have several effects ranging from asymptomatic respiratory tract infection to mild flu-like illness, or to severe lung disease. It is an RNA virus with a viral envelope coated with the Spike protein, capable of binding to the angiotensin converting enzyme 2 (ACE2) to create infection. Coronavirus-19, in addition to causing a dysregulation of the immune system, also provokes severe lung inflammation and fever, mediated

by interleukin (IL)-1 (2). IL-1 shares the same receptor as TLR and is associated primarily with innate immunity, but also intervenes in acquired immunity. IL-1 is used by living organisms for their own immune defense, but when the levels of this cytokine rise outside the physiological state, it becomes highly inflammatory and can be extremely harmful to the body. Infectious microorganisms react with innate immune cells and stimulate the production of IL-1. Both IL-1 and microorganisms can activate TLR receptors, triggering inflammation. Serious infections that induce high levels of IL-1 can lead to death in individuals. Because IL-1 induces other inflammatory cytokines, it can trigger the cytokine storm that also occurs in COVID-19. Infections are characterized by a rapid increase of SAA, the major acute phase reactant in humans and

many other species. IL-1 and IL-6 in combination can act synergistically in inducing serum amyloid A (SAA) (3). IL-1 cytokine causes severe damage to lung tissue and mediates the formation of micro-thrombi. Therefore, IL-1 suppression could be a valid therapeutic strategy to use. The harmful effects due to SARS-CoV-2 have led many laboratories to try to generate a vaccine in order to avoid SARS-CoV-2-induced COVID-19 respiratory disease (4). One of the vaccines made in the short term (less than a year) is that with mRNA that encodes (S-2P antigen) for the spike protein. Vaccination with mRNA is carried out in two doses 21-28 days apart, the first being injected at a higher dose that usually causes an insufficient and unsatisfactory antibody response (Table I) (5). After the second administration, there is a high production of neutralizing serum containing IgG antibodies against the spike protein. Usually these antibody responses to the SARS-CoV-2 virus are equal to or greater than the convalescent serum values. Hence, the mRNA vaccine induces anti-SARS-CoV-2 immune responses, demonstrating its efficacy, and for this has been approved by the Food and Drug Administration (FDA) (6). The vaccine also acts on the stimulation of CD4⁺ T cells and throughout the TH1 cytokine network and,

to a lesser extent, TH2 (IL-4 and IL-13) (7). The mRNA vaccine, supplied with a capsule composed of 4 lipids, has the S-2P antigen which stimulates the IgG antibody. All this together is placed in a sterile saline solution ready to be injected, with the aim of inducing immunity. In general, the mRNA vaccine does not cause serious adverse events, although, in sporadic cases, after the second vaccination, pain at the injection site, transient urticaria, headache, local and systemic allergy, transient fever, fatigue, nausea, swelling, chills, and muscle aches can occur. In these cases, taking analgesics or antipyretics before or after vaccination, could be helpful. After the second vaccination there is an evident and satisfactory increase in the title of the IgG antibodies bound to the S-2P antigen, without any serious toxicity. The mRNA vaccine is already in use globally and has not produced any relevant side effects so far (8). The real question is whether the mRNA vaccines in use today work against the mutated virus.

English variant

After SARS-CoV-2 infection, it is difficult to predict the degree of protective immunity, and it is not yet known whether individuals have a chance to become infected again. It is possible that if the patient has a first infection with SARS-CoV-2 virus, with generation of specific antibodies, and subsequently reinfection with a genetically different virus (high variant), the patient may be unprotected. Therefore, individuals already infected the first time should adopt the usual precautions to avoid reinfection. The English variant was found in the USA and carries the same mutation, but in addition to this, other mutations of which little is known have been discovered and are being studied. The gene sequence of the SARS-Cov-2 virus allows to monitor the evolution of the virus (9). The mutations on the surface of the virus can be different, even if they do not belong to the English variant, and appear in different points of our planet. However, these all seem to have the characteristics of making the virus faster in transmission and more contagious. It is important to continue to monitor the evolution and transmission of SARS-CoV-2 in order to control its impact on health and on the therapy to be implemented.

Table I. Comparison of two RNA vaccines

Pfizer-BionTech

Already authorized by FDA
95% efficacy
Two doses: 21 days apart
Storage -80°C to -60°C

Administration at age 16 years and over

Moderna

Already authorized by FDA
94.5% efficacy
Two doses: 28 days apart
Storage -25°C to -15°C

Administration at age 16 years and over

In light of the new English variant of the coronavirus-19, some doubts have arisen about the effectiveness of the vaccine. In fact, there is no data to believe that these mutations will impact the efficacy of vaccines already approved by the FDA. To date, based on current knowledge, it can be said that the English variant (D614G gene mutation of the amino acid) does not harm the vaccine although it could potentially make it a little less effective (10). However, there is no doubt that the benefit obtained from the anti-SARS-CoV-2 vaccination is enormously greater than the risks and provides a new therapeutic weapon against the deadly COVID-19 disease that now afflicts the populations of our planet. Coronavirus variants are nothing new at all, this is what happens every year with seasonal influenza. For example, it has been noted that the spread of cases of the English variant could be 70% higher than the Sars-Cov-2 virus we know, with an R index growth of 0.4. What we know today is that the viral variant is more transmissible, but it is not yet known whether it is more pathogenic, for this reason new laboratory data are awaited. Fortunately, today vaccines also work for the English variant and induce the formation of specific antibodies that fight the virus. However, if the variants are excessive, current vaccines may not work. In this case the vaccine would need to be updated, as occurs with seasonal influenza. It should be noted that the mutation occurs at the level of the N501Y genome of the spike protein, an alteration of the important part of the virus, that is, the one that binds to the receptor of the host cell. However, as already mentioned, there is currently no evidence that this variant is more dangerous than Sars-Cov-2. What can be said is that any increase in transmission and speed of the viral variant could pose a problem for the health system which is already suffering. The lack of other information on the English variant suggests that this is a subject still under study. Therefore, more in-depth work is needed to investigate the exact role of the English variant and other SARS-CoV-2 variants that are sure to appear in the near future, in order to radically combat this terrible, frightening and deadly disease called COVID-19.

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