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Medicina Clínica 156 (2021) 500–502

MEDICINA CLINICA

www.elsevier.es/medicinaclinica

Editorial

The COVID-19 vaccination☆

La vacunación de la COVID-19

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It is now one year since the SARS-CoV-2 coronavirus pandemic, which has caused so many cases and so many deaths worldwide, was declared. As of 12 February 2021, WHO estimates 105,429,382 cases and 2,302,614 deaths.[1] In Spain, 3,056,035 cases have been reported, with a total of 64,746 deaths.[2] The pandemic is causing a serious health, social and economic crisis in the world. It has shown the weakness of health systems and public health agencies when it comes to providing a rapid and appropriate response to an unexpected situation. The collapse of health centres has made it difficult to provide proper care for patients with other diseases, as was the case before the pandemic, such as the delay in surgical interventions, or the effect on vaccination coverage in both children and adults,[3] to name a few examples. On the other hand, there has been no investment in other diseases that are important from a public health perspective, such as the fight against tuberculosis. According to the "STOP Tuberculosis Alliance", it is thought that we may have lost up to 8 years in the prevention and control of this disease due to the COVID-19 pandemic.[4]

While experts have generated a significant amount of evidence on the morphology of the virus, the mechanisms of transmission and the associated clinical symptoms, there are still many aspects that are not fully resolved, such as the origin of the virus, how it came to infect the first human, or the appropriate therapies to address the disease.

Our lives have changed compared to how they were before the pandemic. One of the hopes we currently have is to provide safe and effective vaccines to the population. These vaccines are intended to achieve herd immunity to break the chain of transmission. This herd immunity depends on many factors, one of them being the basic reproduction number or Ro, which is the average number of secondary cases generated by an infected case. This Ro is calculated to be between 2.5–3.5, so it is estimated that 60–72% of the population needs to be immunized to achieve this population "shield".[5]

Since the emergence of this disease, more than 250 groups in the world have been working on the development of these vaccines.[6] As of 12th February 2021, there are 66 vaccines in the clinical phase, of which 21 are in phase 3 and 176 in the preclinical phase. One thing most of these vaccines have in common so far is that they are all designed to elicit an immunogenic response against the S or Spike protein of SARS-CoV-2.

Currently, the European Medicines Agency has approved 3 vaccines for use in the European population. The Comirnaty vaccine® (Pfizer/BioNTech) was approved on 21st December, Moderna® on 6th January and AstraZeneca® on 29th January 2021. The 3 vaccines have shown adequate levels of safety and efficacy, although they present differences in terms of their logistics, their efficacy and the population groups that have been included in the trials.

The first 2 licensed vaccines, Comirnaty® and Moderna®, have a very similar mechanism of action, using messenger RNA platforms encapsulated in a lipid coating to facilitate their entry into the cell. This mRNA instructs the cell to make protein S, and then it disintegrates rapidly, without integrating into our DNA. The AstraZeneca vaccine® uses vector platforms, specifically a chimpanzee adenovirus that carries the genetic material necessary to encode protein S inside human cells.

The efficacy shown in clinical trials is very similar in all of them, being 95% and 94% in the two mRNA vaccines, without significant differences between the different age groups, and between 62.1% and 90% in the AstraZeneca® vaccine. In the latter vaccine, the population over 65 years of age was under-represented in clinical trials, which is why it is reserved for the population under 65 or 55 years of age, depending on the European country. All consist of a 2-dose regimen, with the second dose after 21 days for Comirnaty®, after 28 days for Moderna® and between 10 and 12 weeks for AstraZeneca®.[7–9]

The vaccination strategies against COVID-19 in Europe and in Spain establish that, taking into account the progressive availability of doses, it is necessary to carry out a prioritization exercise according to ethical principles and risk criteria.[10,11] In the first stage, priority has been given to reinforcing the protection of the most vulnerable and those who have a higher risk of exposure: residents and staff in nursing homes, health and social care personnel and non-institutionalized severely dependent individuals.

Currently, according to the Ministry of Health website, as of 12 February there are 2,914,755 doses distributed, 2,423,045 doses

☆ Please cite this article as: Casas I, Mena G. La vacunación de la COVID-19. Med Clin (Barc). 2021;156:500–502.

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administered (83.1% of the doses received) and 1,000,485 people with the completed regimen (41.3% of the doses administered).[11]

None of the available vaccines are made up of attenuated viruses, therefore they cannot replicate and cause disease. For this same reason, they can be safe during pregnancy and breastfeeding, although for the moment, in the absence of evidence, their administration during pregnancy is not recommended unless they belong to a group at risk of exposure (such as health personnel) or a group at high risk of complications, evaluating the risk/benefit in all these cases. There is also no reason for termination of pregnancy if the vaccine has been inadvertently administered.

The first report of the Spanish Agency of Medicines and Medical Devices confirms that there have been no serious side effects in vaccinated patients, and this is very important in the field of vaccination.[12] Most of the side effects are mild systemic or self-limiting local reactions, such as fever and headache that appear in the first 24–48 h and resolve within 2 to 3 days. Reactions seem to be more frequent with the second dose and in people under 55 years of age.[13,14] For the time being, caution should only be exercised in people with a history of allergy, especially to parenteral medication.

So far, no safety concerns have been found in patients with a history of having had the disease. For prioritization reasons only, it is recommended to delay vaccination 6 months for health and social care workers under 55 years of age.[11]

They also cannot be administered to young people under 16 or 18 years of age, depending on the vaccine and the trial population, as safety and immunogenicity data are not available. One piece of information for optimism is that trials in these populations have already begun.

The protective immunity generated by the vaccine can appear 10–14 days after the first dose, although optimal protection is not guaranteed until 7–10 days after the second dose.[8] It should be borne in mind that the incubation period of the disease is very long and, even if there are no symptoms at the time of vaccination, symptoms may appear days after vaccination. Therefore, after a dose of vaccine has been administered, the disease may develop, but this does not mean that it was caused by the vaccination.

Another much disputed uncertainty is whether we can lengthen the intervals between doses as established in clinical trials. An important clinical practice premise in vaccinology is that there are minimum intervals between doses that must be observed, but there are no maximum intervals. There has been talk of delaying the second dose because of the delayed inclusion of the vaccinated population, especially while the pandemic is at high levels. Experience with other vaccines has taught us that a vaccine given at a longer interval than the established interval would also be effective. Furthermore, there is also the question of whether a single dose would be sufficient in cases with a history of previous infection. A study carried out in Israel has shown that healthcare workers with a history of previous infection had higher post-vaccination antibody titres than individuals without a history of previous infection, regardless of the presence of detectable antibodies before vaccination.[15] As long as vaccines are available, it seems sensible to continue with the guidelines established in clinical trials.

We know that RNA viruses mutate very easily and, although coronaviruses have the fewest mutations, SARS-CoV-2 has undergone small genetic variations. We do not know if current vaccines will protect against new variants of this virus. For this reason, and because the duration of immunity generated by current vaccines is unknown, it is not unreasonable to envisage a scenario of regular revaccination, as is the case with influenza vaccination.

Another important question is whether the vaccine will protect against asymptomatic infection and thus prevent transmission. It is a highly debated topic, since we still do not know the effect of existing vaccines on the production of IgA antibodies, which would protect against upper respiratory tract infection, nor if the presence of IgG antibodies created by immunization would reduce the amount and the duration of viral secretion. Studies in Israel show that the first dose of vaccination with Comirnaty® reduces the viral load of subsequently infected individuals.[16] If this is confirmed, the spread of the virus would decrease and there would be greater control of the pandemic when high vaccination coverage is achieved.

Regarding immunogenicity, it is important to note that healthy populations or those with non-decompensated comorbidities have been included in clinical trials. Therefore, we can find differences between the efficacy found in clinical trials and the effectiveness of the vaccine currently being administered to elderly or severely immunosuppressed populations.

Although there have been studies that show that acceptance is high both in health personnel and in the general population, it should be noted that 15–20% of the population has many doubts about the safety of the vaccine.[17] These doubts are probably due to a lack of information. For this reason, it is particularly important to convey messages to the population in a clear and precise way, so that they understand the need to be vaccinated. Safety concerns are mainly related to the speed with which these vaccines were approved. These vaccines have been produced in a shorter time than other vaccines for several reasons: (a) we were not starting from scratch, as we have used known and previously used technologies; (b) it has been possible to overlap different phases that are normally sequential; (c) the recruitment stage, which in many vaccines takes a long time, has been shortened here due to the ease of inclusion of volunteers, and (d) the global emergency has led to a significant contribution of public and private funds.[18]

Added to the difficulty of vaccine development is the complexity of vaccine distribution, storage, and administration, which is why the more vaccines we have approved, the faster the entire population will be immunized.

Finally, it should be noted that it is important to reduce the inequalities in the distribution of vaccines around the world, especially if we are to achieve herd immunity. Moreover, the consequences of COVID-19 infection in countries with weak health systems are much more devastating. Vaccines are now the great hope for ending this pandemic, but we must not let our guard down on our current prevention measures until, at the very least, we have achieved herd immunity. In other words, appropriate use of facemasks, hand hygiene, avoidance of enclosed and crowded places, and social distancing should continue. We now have the opportunity to urgently consider strengthening public health in order to be better prepared for possible future challenges.[19]

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