Update on the management of SARS-CoV-2 infection

Vaccination strategies against SARS-CoV-2: General impact on the development of the pandemic

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ABSTRACT

In this article, we will review the main vaccination strategies currently being implemented by the health authorities and analyze the main vaccines authorized by the EMA. As practical aspects of vaccination, we must make it clear that until collective immunity is reached, the preventive measures being implemented will have to be kept in place. In the words of the WHO Accelerator Project, “There is no time to waste in the fight against COVID-19. No one is safe until everyone is safe.”

Keywords: COVID-19 pandemic, vaccine, vaccination strategies, herd immunity, mRNA technology, adenoviral vectors.

Vaccination strategies against COVID-19 are part of the scope of responsibilities of the COVID-19 Vaccination Working Group of the Inter-Territorial Council Vaccination Communications and Registry, and up to the time of writing this article, five previous updates have been published. This is clearly a topic of great current importance but also subjected to continuous change. In fact, from February to the present date, there have been important changes, and it is possible that when this monographic issue is published, additional changes will have been made, including a possible 6th update of the vaccination strategy.

In this article and before going into the specific details of the vaccination strategy, we will briefly review concepts we have heard in the media and that have become colloquial, although they are possibly not always sufficiently clear. The first of these is collective, group or herd immunity. Underlying these three terms – collective, group or herd – is a concept and, at the present time, a need to achieve the greatest possible proportion of immunity in a given population, either by natural immunity – in which the majority of the population contracts the disease – or by artificial immunity, that is, by vaccination of the population. As is logical in the face of COVID-19, all people were initially vulnerable, and after a year of the pandemic, we have barely reached 25% collective immunity in areas with a higher cumulative incidence of the disease. Thus, it is necessary to reinforce that immunity through vaccination to reach the highest possible vaccination coverage is the only way to ensure adequate control of the pandemic. Therefore, the other relevant concept is vaccination coverage; considering that the majority of the population is susceptible to acquiring the disease, it is logical that this coverage must be close to 100%. That is, the main objective, as indicated by the Ministry of Health, is “to reduce the morbidity and mortality caused by this disease through vaccination against COVID-19, in a context of increasing availability of doses and protecting the most vulnerable groups”. In Spain, from December 27 to April 1, nearly 8 million vaccine doses were administered, with already noticeable results in reducing hospitalizations and deaths [1,2].

Therefore, it is necessary to have safe and effective vaccines produced on a large scale because the majority of the population must be vaccinated, and any strategy must protect the most vulnerable. In fact, from February to the present date, there have been important changes, and it is possible that when this monographic issue is published, additional changes will have been made, including a possible 6th update of the vaccination strategy.
vaccines have been produced at the manufacturers’ risk while clinical trials were still underway, and the vaccines were authorized knowing that data from completed phase III trials will only be available by the end of 2022. The need to have vaccines available and reduce morbidity and mortality due to COVID-19 led to faster approval, but all vaccines are subject to review and changes in technical specifications according to the what the results of vaccinating the population show.

As mentioned, several vaccines have been authorized, but we will comment only on some of the data from those that were approved by the European Medicines Agency (EMA), i.e., four vaccines, two that use mRNA technology and two that use adenovirus viral vectors.

The first of these is the Pfizer/BioNTech BNT162b1 and BNT162b2 or Comirnaty vaccine. Clinical trial results were published in The New England Journal of Medicine (NEJM) at the end of 2020 [4]. It is an mRNA vaccine that, once administered, encodes the S protein fragment of SARS-CoV-2; given that mRNA is very sensitive to temperature, this vaccine has to be kept between -70-80 °C, which requires special logistics, which initially was assumed to be a complication but that, at the present time, has been solved. The vaccination schedule includes two doses, 3 weeks apart. These aspects have been changed in the fact sheet, as it has been shown that the thermostability and conservation of the vaccine have improved. Other aspects to highlight are its efficacy, approximately 95% with a 95% confidence interval (CI) between 90-97%; 14 days after the first dose, individuals are up to 90% protected, but there are still no data to allow single-dose vaccination schedules. Regarding efficacy, it should also be noted that in addition to good immunogenicity, the vaccine triggers a robust cellular response mediated by CD4+ and CD8+ cells with a Th1-polarized profile, which has great value because it indicates that the vaccine generates good memory immunity. Regarding reactogenicity, the vaccine has been well-tolerated in all age groups, although greater reactogenicity is observed after the second dose, and after some allergic reactions were reported, the decision was made to contraindicate it for people with a history of severe allergic reactions to any of the vaccine components.

The second vaccine is the Moderna mRNA-1273 vaccine, whose phase III results were also published in NEJM [5]. Similar to the previous vaccine, this vaccine also uses mRNA encoding the S-2P glycoprotein, in this case consisting of the S protein stabilized in its prefusion conformation by two consecutive proline substitutions at positions 986-987. Additionally, the mRNA is encapsulated in lipid nanoparticles. The vaccination schedule is two separate doses, in this case 4 weeks apart, and it also shows thermostability at -70-80 °C. Regarding efficacy, it also exceeds 94% (95% CI 89-97%) and has good immunogenicity with a robust cellular response, producing CD4+ neutralizing antibodies with a Th1 cytokine profile. This vaccine has a good safety profile, and similar to the previous one, adverse effects are stronger after the second dose.

The third authorized vaccine, Oxford/AstraZeneca ChA-dOx1/AZD1222, is a viral vector vaccine based on the complete S glycoprotein of SARS-CoV-2 that is vehicularized in an adenovirus, the chimpanzee adenovirus ChAdOx1. Clinical trial data were published in NEJM, and there was a subsequent publication with updated efficacy data in the Lancet [6,7], indicating 76% efficacy after the first dose and 82% after the second dose (95% CI 63-92%). Additionally, after an exhaustive review of the published data, it has been considered that the best vaccination schedule is to administer a second dose 12 weeks after the first dose. The vaccine has good thermal stability that allows storage between 2-8°C. Regarding safety, similar to the other vaccines, there is local and general reactogenicity that increases after the second dose. In the phase III trial, some participants used paracetamol to prevent some symptoms; therefore, the possibility of using paracetamol as a preventive measure for some symptoms, such as local pain, is included in the fact sheet. Notably, some adverse vascular effects have been recently reported, such as thromboembolism, at a frequency of 1 case/1 million doses administered, and these have been analysed by the EMA, but a causal relationship has not been established. The vaccine shows good efficacy after the second dose, and good immunogenicity and a cellular response with memory immunity have been quantified.

Last is the Janssen vaccine, based on human adenovirus 26 as a non-replicating viral vector containing the complete S glycoprotein, with an acceptable safety profile and lower reactogenicity in those over 65 years of age. The regimens tested were 1 and 2 doses, and it was found that a single dose is effective for all participating population groups; thus, it was decided to indicate only one dose. Its efficacy is 67% (95% CI 59-73%) for all study participants, maintaining this level in all groups studied by age and comorbidities. As a critical fact, the impact of vaccination with a single dose on hospitalizations and deaths has been very beneficial. Therefore, its data sheet highlights the protective effect against moderate, severe (up to 72%) and critical (up to 86%) forms of COVID-19. Regarding thermostability, the vaccine can be stored between 2-8°C. Finally, regarding safety, its profile is comparable to those for the other currently authorized vaccines [8].

There are still many questions about vaccines that will be answered with time, but the research has not stopped nor will it stop because there are many unknowns to be resolved. New trials are underway to determine the efficacy of the current vaccines against new variants of the virus, and the results obtained are encouraging, especially against the British strain for most vaccines and against the South Africa and Brazil strains for some of them; much remains to be investigated and advanced regarding this aspect, and in the coming months, we will surely have more information [9].

Recently, in the last document updating the vaccination strategy, the Ministry of Health provided data on vaccine effectiveness that show that in the cohort study being carried out, 52% of vaccinated participants were protected after the first dose administered; this rate was 71% for the Comirnaty vaccine. In turn, in the study that used the screening method,
64% of vaccinated participants were protected with the first dose, with an effectiveness in reducing hospitalizations of 26% and reducing deaths of 35%; at 7 days after the second dose, 88% of the vaccinated participants were protected, with an effectiveness in reducing hospitalizations of 77% and reducing deaths of 87% [1,2].

In conclusion, as practical aspects of vaccination, we must make it clear that until collective immunity is reached, the preventive measures being implemented will have to be kept in place. In the words of the WHO Accelerator Project, “There is no time to waste in the fight against COVID-19. No one is safe until everyone is safe.”

CONFLICTS OF INTEREST

The authors declare no conflict of interests.

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