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Editorial

SEPAR recommendations and new challenges on COVID-19 vaccine in respiratory diseases

Recomendaciones SEPAR y nuevos retos sobre la vacuna contra la COVID-19 en las enfermedades respiratorias

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The scientific community realised that mass vaccination of the population was the best tool to combat SARS-CoV-2 from the moment it was declared a pandemic. After a great effort, several vaccines were developed in less than a year, some using very new technology. Given their limited availability, the Council of the Spanish National Health System proposed from the outset a vaccination strategy based on the age and risk of the population, aimed primarily at reducing mortality, transmissibility, and the burden on essential services. Priority was given to vaccinating nursing homes, healthcare workers, essential service workers, and people with severe disabilities.1

This strategy has been adjusted to the availability of vaccines, progressively prioritising patients with oncohaematological diseases, immunosuppression, or dialysis.2 However, patients at high-risk for an unfavourable outcome, with chronic respiratory diseases, cardiovascular diseases or obesity,3 for example, are left for later stages. Moreover, the onset of various side effects has generated the need to identify risks and contraindications of this vaccination, especially in the most vulnerable patients.

Therefore, the Spanish Society of Pneumology and Thoracic Surgery (SEPAR) has drawn up a document to help healthcare personnel in vaccinating patients with respiratory diseases.4 Experts in pulmonology, thoracic surgery, nursing, microbiology, immunology, preventive medicine, epidemiology, and public health participated. A literature review was conducted for the three compounds that had been approved at that time: Pfizer/BioNTech, Moderna and AstraZeneca. The document reviews their main characteristics, analyses the global vaccination strategy proposed by the Ministry of Health and emphasises the important role of pulmonologists in achieving good adherence and vaccination coverage in patients with respiratory diseases. Finally, we give a series of recommendations for the management of the COVID-19 vaccine in different respiratory and thoracic diseases, acute and chronic, that make the patient especially vulnerable to SARS-CoV-

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| Respiratory disease                                                                 | Recommendation                                                                                                                                                                                                                                                                                                                                 |
|----------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Previous SARS-CoV-2 infection                                                    | Patients with a history of confirmed previous SARS-CoV-2 infection should be vaccinated according to the current recommendation. Vaccination in previously infected patients could be delayed for six months and be done in a single dose. Warning about a potentially intense post-vaccination reaction in subjects infected less than six months earlier. |
| Current respiratory infection                                                    | Vaccination should be postponed in people with severe acute febrile illness ($\geq 38^\circ$ C) or acute infection. The presence of mild infection and/or low-grade fever should not postpone vaccination. Administration of the SARS-CoV-2 vaccine is advised in patients with allergic asthma with sensitisation to inhaled allergens (dust mites, pollens, animal epithelia, fungi), as there is no evidence to the contrary. Patients with severe asthma treated with biological drugs can receive the SARS-CoV-2 vaccine, but it is advisable to delay administration of the biological agent for 5–7 days, essentially as surveillance for possible adverse effects after vaccination. Patients with severe asthma treated with biological agents could be a priority group for the vaccine, as recent studies have observed worse COVID-19 disease progression in this subgroup. The SARS-CoV-2 vaccine should not be administered to patients with a history of anaphylactic reaction to biological drugs. |
| Severe asthma                                                                    | Patients with COPD should be a priority group for vaccination against SARS-CoV-2. Patients with Alpha-1-antitrypsin deficiency (AATD) should be a priority group for vaccination against SARS-CoV-2. Neither smoking, COPD treatment nor replacement therapy for AAD is a contraindication for vaccination against SARS-CoV-2. It seems common sense not to recommend vaccination during flare-ups, regardless of the severity of the flare-up. |
| Stable and acute COPD                                                            | Patients with bronchiectasis treated with biological drugs can receive the SARS-CoV-2 vaccine, but it is advisable to delay administration of the biological agent for 5–7 days, essentially as surveillance for possible adverse effects after vaccination. Patients with severe asthma treated with biological agents could be a priority group for the vaccine, as recent studies have observed worse COVID-19 disease progression in this subgroup. The SARS-CoV-2 vaccine should not be administered to patients with a history of anaphylactic reaction to biological drugs. |
| Bronchiectasis and chronic bronchial infection                                   | Preventive antibiotic, steroid or other treatment prior to vaccination is not necessary. Any basic treatment regimen should not be changed because of vaccination. During a flare-up, it is reasonable to wait for the process to stabilise before proceeding with vaccination. |
| Pulmonary hypertension                                                           | Vaccination against COVID-19 is recommended in patients with pulmonary hypertension. It is recommended that COVID-19 vaccination should not be administered during episodes of decompensation of pulmonary hypertension. Patients with pulmonary hypertension receiving anticoagulant therapy should not discontinue anticoagulant therapy, but should take precautions. |
| Pulmonary thromboembolism and anticoagulant therapy                              | Anticoagulant therapy does not contraindicate vaccination against COVID-19. It is recommended not to administer COVID-19 vaccine in the acute phase of pulmonary thromboembolism. |
| Cancer under active treatment                                                    | Vaccination is recommended in patients with advanced cancer, especially those diagnosed with lung cancer under active treatment. There are no data to support patients with a history of cancer being prioritised for vaccination. Other risk factors should be considered. There is no contraindication to vaccination while undergoing cancer treatment, but vaccination is recommended before starting treatment. |
| DILD and anti-fibrotic or immunosuppressive therapy                              | Patients with diffuse interstitial lung disease (DILD), especially those with fibrosing DILD, are at high risk for severe infection and should be prioritised for vaccination against SARS-CoV-2. There is no evidence of interaction with antifibrotic medication, and therefore the usual treatment regimens should not be modified, either before or after vaccination against SARS-CoV-2, as is the case with influenza or pneumococcal vaccination in these patients. During a flare of DILD, it is reasonable to wait for the process to stabilise before proceeding with SARS-CoV-2 vaccination. In patients with DILD associated with systemic autoimmune diseases and immunomodulatory treatment, vaccination against SARS-CoV-2 is recommended, with attention to patients on treatment with B-cell depleting antibodies, preferably administered before planned immunosuppression or away from the infusion. |
| Lung transplantation                                                              | Vaccination against COVID-19 is recommended in lung transplant recipients and candidates on the waiting list. |
2 infection (Table 1). The paper concludes that COVID-19 vaccines are not only safe and effective, but are even a priority in vulnerable patients with chronic respiratory diseases. We are therefore left with the challenge of immunising this large population, as the availability of the vaccines is still limited.

The efficacy of vaccines against new strains of the virus is another area of uncertainty. RNA viruses, such as SARS-CoV-2, tend to mutate in successive replication cycles due to errors in RNA-copying enzymes. Although this may suggest a threat to vaccine effectiveness, its impact on vaccine efficacy must be put into context. First, although some strains appear to be more infectious because they have a higher viral load in the upper respiratory tract, they do not always result in more severe infection. Some authors argue that the mutated strains currently circulating have not had a major impact on the course of the pandemic. Secondly, vaccines generate an immune response usually involving a wide range of antibodies, and preclinical models have shown that mRNA vaccines produce antibodies that block the mutated viruses better than the original viruses. Growing concerns about the potential transmissibility, virulence and ability of new variants to undermine the efficacy of existing vaccines are an argument in favour of accelerating mass vaccination of the population.

The obstacles to achieving this goal range from denialism, vaccine shortages, onset of side effects with continuous interruptions of administration, storage requirements or uncertainty about the duration of immunity. Vaccine shortages generated debate about prioritising a single dose to more people or even spacing doses. It should be noted that mRNA vaccines can become dose-dependent, requiring the integration of genetic information into the immunity cells. Removing patents to increase production is an unresolved debate, although the production of preparations with exactly the same formulation and quality in all batches should be ensured.

Reports of serious cases of thrombosis associated with certain vaccines raised questions about their use in patients with conventional risk factors for thrombosis. However, as they act by an immune mechanism, no restrictions are envisaged in this regard. Nor is it currently possible to determine the risk factors for this adverse reaction, although because of their similar pathogenesis they are not recommended in people with a history of heparin-induced thrombocytopenia. There is a question as to the efficacy, efficiency, and safety of combining vaccines with different mechanisms of action.

As we wait for science to resolve all the uncertainties surrounding the COVID-19 vaccine, new challenges are emerging, including whether global vaccination will be sufficient to eradicate this unexpected pandemic, or whether we will have to live with the virus forever.

**Conflict of interests**

The authors have no conflict of interests to declare.

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**Table 1 (Continued)**

| Respiratory disease | Recommendation |
|---------------------|----------------|
| Chest surgery       | Vaccination should be performed at a time when the underlying disease is stable, and baseline immunosuppressive treatment regimens do not need to be modified. Emergency surgeries should take place regardless of vaccination status. It is recommended to schedule the vaccination process and the elective surgical procedure so that neither are delayed, separating them by a maximum of one week, respecting the dose intervals and individualising them in the case of immunodeficiencies. |
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