Safety of new MRNA Vaccines Against COVID-19 in Severe Allergic Patients

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The coronavirus disease 2019 (COVID-19) pandemic is a global crisis, with devastating impacts. Safe and effective vaccines are needed to prevent disease caused by the new coronavirus Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Two mRNA vaccines were approved in the last days of 2020: Comirnaty® (Pfizer-BioNTech) [1], and COVID-19 Vaccine Moderna® (Moderna) [2].

During the first days of the vaccination campaign, few cases of anaphylaxis after the administration of both vaccines, in patients who had a known history of severe allergies, were reported. An alert was triggered by different regulatory organisms to contraindicate their administration to allergic patients, without clear specific indications, in terms of allergy [3,4].

Confirmed allergic reactions to vaccines are not frequently attributed to the active ingredients but rather to the excipients [5,6]. One of the excipients on both Pfizer-BioNTech and Moderna vaccines is a known potential allergen, the polyethylene glycol (PEG), which is widely used due to its stabilizing properties [7]. Additionally, COVID-19 Vaccine Moderna® also contains trometamol [5].

The aim of this study was to evaluate the ability of a new protocol for selecting patients with previous severe allergic reactions, who could safely receive the vaccines and to detect patients in whom vaccines should be avoided.

Between January and February 2021, during the vaccination campaign against COVID-19, a specific questionnaire was implemented to the healthcare workers from a third level hospital in Madrid (Spain) to select subjects with previous severe allergic diseases. They were sent out from the Occupational Risk Prevention Department to have the vaccination administered in our Allergy Department.

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We recorded data of sex, age, personal history of cardiovascular or respiratory diseases, autoimmunity, immunosuppression, chronic cutaneous diseases, treatment at the moment of the study, and other not severe allergies.

Before the vaccine administration, all patients had skin prick tests (SPT) performed with the vaccine to be administered (dilution 1:1) using the waste of each vial thawed in the previous 6 hours. We also performed SPT with PEG-3350 (530 mg/ml) in patients who were going to receive Comirnaty®, and PEG-3350 and trometamol (10 mg/ml) in those with COVID-19 Vaccine Moderna®. Tests were read at 20 minutes. We administered the first dose of the corresponding vaccine followed by an observation period of 30 minutes.

The study protocols for the clinical data collection were reviewed and approved by the Ethics Committee of our hospital.

A total of 186 subjects were referred to our Allergy Department from the Occupational Risk Prevention Department (Figure 1). After allergist evaluation, 55 patients were discarded for several reasons: not meeting criteria for severe allergic reaction, poorly controlled asthma or non-acceptance of the allergy study. The final study population comprised 131 patients. Their characteristics are summarized in (Table 1 and 2: Repository on line) One hundred and twelve (85.5%) were female, the mean age was 47 (26-66) years old. Twenty-eight (21.4%) patients had cardiovascular disease, 34 (26%) patients had respiratory diseases, 6 (4.6%) immunodepression, 21 (16%) autoimmunity, and 3 (2.2%) chronic cutaneous affections.

Anaphylaxis was the main allergic medical history (121/131, 92.4%), and it was triggered by drugs in most cases (66/121, 54.5%), followed by food (40/121, 33.1%), Hymenoptera sting (4/121, 3.3%), latex (4/121, 3.3%) and others (10/121, 8.3%). In 3

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cases (2.5%), the offending agent was unknown, and 13 patients (10.7%) had anaphylactic reactions triggered by multiple agents.No delayed allergic reactions to the excipients were reported. Of the total of 45 asthmatic patients (34.4%), 9 (20%) had severe asthma. Seven patients (5.3%) were diagnosed with chronic urticaria and 1 patient (0.8%) had mast cell activation syndrome. Thirteen (9.9%) referred contact dermatitis with cosmetics, although only 3 of them (18.8%) had previous allergy studies.

Skin prick test with the mRNA vaccine and trometamol were negative in all cases. PEG-3350 SPT was positive in 2 patients (1.6%) and the mRNA vaccine was contraindicated. Patient 1 was a 27-years-old female, with a history of drug-induced anaphylaxis and one episode of unknown cause anaphylaxis. She related this episode after the intake of a drug containing poloxamer 407 as an excipient, a PEG derivative, with demonstrated cross-reactivity to PEG [8]. Patient 2 was a 39-years-old female, with a history of a perioperative anaphylactic shock during vaginal delivery with epidural anesthesia. The anaphylactic episode remained unresolved after conducting the allergy work-up, but the implication of PEG could not be ruled out.

During the current study, subjects received the first dose of a mRNA COVID-19 vaccine. There was only a mild immediate reaction in a 43-year-old woman with a personal history of severe asthma, 10 minutes after the administration of the BioNTech-Pfizer mRNA vaccine. She developed nasal obstruction and rhinolalia and pruriginous erythematous macules on the neck and upper thorax. Intramuscular dexchlorpheniramine was administered and symptoms resolved within 60 minutes. No modification on tryptase levels compared with the baseline was found.

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Allergy to excipients is often overlooked due to a lack of knowledge about their allergenic potential [5]. However, immediate hypersensitivity to PEG has been reported, including life-threatening allergic reactions [9]. We identify 2 patients with positive PEG-3350 SPT and both had a history of unknown cause anaphylaxis which could be related to PEG derivates. Although the positive predictive value of the SPT with PEG is not already known, as it is a hidden high-risk and widely spread allergen [8,9], we recommend avoiding these vaccines in patients with a positive test.

We proposed herein a questionnaire and an allergologic study able to select patients with severe allergic reactions that could safely receive the Comirnaty® (Pfizer-BioNTech) or COVID-19 Vaccine Moderna®. In the present study, 99.22% of subjects with previous severe allergic diseases tolerated mRNA vaccination with no reaction in 128 out of 129 vaccines administrated.

Allergy practitioners must ensure reliable alternatives for their allergic patients in support of the COVID-19 vaccine rollout programs [10]. We recommend that all allergic patients be screened by a straight questionnaire to determine the possible risk for an allergic reaction to the mRNA COVID-19 vaccines. We must continue working in the search for solutions that allow safe vaccination procedures during this unprecedented immunization strategy.

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Figure 1. Patient flow diagram and outcomes of allergy work-up.