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Allergists and COVID-vaccine: which is the actual risk of reactions in allergic patients?

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To the Editor,

The global vaccination campaign against SARS-CoV-2 started over one year ago: pictures of the first vaccinated patients sparked hope in the population, but also some concerns among allergists and allergic patients, as the first reports of allergic reactions, even severe, emerged after the first days of the campaign (1).

In the subsequent days and months, position papers by various scientific societies pointed out the importance of the vaccination even in the allergic subjects, who should not be excluded from the vaccination campaign (2, 3), while researchers tried to define the risk of allergic reactions to mRNA covid vaccine and their potential mechanisms, highlighting the supposed role of Polyethylene glycol (PEG) (4) and the possible role of skin tests in diagnosing sensitization in patients with suspected drug-allergy or after immediate vaccine reactions (5). The next months have shown the schedules of allergist and allergy clinics, filled all over the world with appointments for pre-vaccination consultation and post-vaccination visits in patients with reported reactions, these issues being usually faced by pediatric allergists.

In our allergy clinic in the Hospital of Parma we took care of the evaluation and subsequent vaccination of patients allergic to latex, foods (patients with history of moderate to severe reactions to lipid transfer proteins (nsLTP) or storage protein), drugs (mainly patients with history of anaphylaxis to antibiotics, contrast agents and chemotherapy) and Hymenoptera venom (patients with previous anaphylaxis from Hymenoptera stings and patients undergoing venom immunotherapy) as well as with mastocytosis and asthma. We also evaluated patients referred to our clinic after immediate and delayed reactions to covid-19 vaccine.

As for food (over 150 patients) and Hymenoptera venom allergic patients (almost 250 patients), most were vaccinated without reactions. Reported reactions were those commonly described also in the non-allergic population: itching, urticaria, angioedema, chest tightness or shortness of breath.

Concerning drug allergic patients (over 500 patients), we observed a difference in the risk of allergic reactions depending on the drug causing the first reaction and the type of the reaction: in fact, while patients with history of reaction to chemotherapy (mainly to platinum and paclitaxel) and contrast media showed no significant higher risk of reactions (it has to be noted that our hospital used mainly the Pfizer-BioNTech vaccine, not containing trometamol, in the first eight-nine months of the vaccination campaign), patients with a history of allergic reactions to antibiotics showed higher incidence of immediate reactions such as angioedema, urticaria and respiratory symptoms.

Over the thirteen months of vaccinations, we treated three severe reactions, all after the first dose (with Comirnaty/Pfizer-BioNTech): one patient with anaphylactic shock (positive history for anaphylaxis following beta-lactam administration), one patient with moderate hypotension, hives and wheezing (positive history for anaphylaxis after administration

of contrast media) and one patient with severe bronchospasm and itching. All the patients were treated with adrenaline immediately after the onset of the symptoms; two of them were transferred to the emergency department for subsequent observation and none of them required further hospitalization.

As for the patients referred to our allergy clinic for immediate reaction following administration of the first or second dose, only in a small fraction (6 of almost 150 patients) we could prove PEG hypersensitivity. To these patients we proposed further vaccination using the Johnson&Johnson vaccine: three of them agreed and were vaccinated without further reactions.

The majority of the patients with no evidence of PEG hypersensitivity agreed to the second (or third) dose; in most cases the reaction following the vaccination was similar or milder to the previous one, less frequently more severe (the three aforementioned patients with severe reactions were not administered the second dose given the severity of the reaction).

About delayed reactions, the most common were urticaria (more frequent for the Pfizer-BioNTech vaccine), typically resulting in spontaneous resolution or after a brief course of antihistamine therapy, and large local delayed reaction (the so-called "covid-arm" (6), which had higher incidence in patients vaccinated with the Moderna vaccine. In a fraction of these patients, we opted to perform skin tests, mainly in patients with reactions occurring between two to six hours after the vaccination and in moderate to severe reactions (persistent urticaria or intense dermatitis), not only to exclude hypersensitivity to PEG, but also to reassure the patient and encourage the consent to the second or third dose of the vaccine.

Globally, we observed higher incidence of immediate reactions in female gender, mainly consisting of itching, hives and angioedema, occurring within the first hour of administration; in older patients (over 65 years) the most common reactions were instead itching and angioedema, occurring some hours after the vaccination. The rate of immediate reaction in our patients were higher in patients with history of allergic conditions, mainly drug allergy.

A recent review analysed the present and future perspectives of the COVID-19 Vaccine in the United States and United Kingdom, realizing that the lessons learned so far will allow us to better understand these vaccines and make the right decisions (7).

After over one year of vaccination, after direct experience on high numbers of patients, we can say that the available vaccines are safe and effective for allergic people as much as they are for the general population. However, as the vaccination campaign goes on, we must not forget that in a fraction of allergic patients there may be a risk of hypersensitivity reactions.

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