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Nonirritant concentrations for skin testing with SARS-CoV-2 mRNA vaccine

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Clinical Implications

- Skin testing (prick test and intradermal test) can be performed with the Pfizer-BioNtech severe acute respiratory syndrome coronavirus 2 vaccine, up to the undiluted form, without the risk of eliciting an immediate irritant reaction. This finding can help the evaluation of patients with an immediate reaction to the first dose of the vaccine or with a suspected immediate reaction to a component of the vaccine and who require vaccination due to the coronavirus pandemic.

The importance of vaccination to the coronavirus disease 2019 pandemic cannot be understated. However, reports of anaphylaxis associated with the Pfizer severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine are emerging with the beginning of large-scale vaccination.[1] Preliminary data suggest an incidence of anaphylaxis of approximately 1 in 100,000 injections, 10 times greater than the incidence of traditional vaccines. Hypersensitivity to the vaccine, or to one of its components, has generally been established as a contraindication to the vaccine administration.[1]

Concerning the observed anaphylactic reactions, the pathophysiology remains to be determined. An IgE-mediated pathway must be considered. Polyethylene glycol (PEG) 2000, used as a stabilizer of the lipid-based nanoparticle carrier system of the Pfizer SARS-CoV-2 vaccine, has been pointed as a possible culprit, and its role in inducing IgE-mediated anaphylaxis is well documented.[1,2] Therefore, skin testing with the vaccine may prove a valuable method to evaluate patients who experienced immediate reactions with the first dose of the vaccine, as well as to identify people with allergy to the vaccine or its components and who should avoid it. The biggest problems in using the vaccine is the lack of information concerning the adequate (nonirritant) concentration for the skin tests,[3] and the need for additional vaccine to perform the tests, especially considering the need for a quick worldwide vaccination and the consequent scarcity of the vaccine.

Pfizer's specifications regarding the vaccine use state that each vial contains enough for 5 doses with a 6-hour viability before inoculation. In some settings, health care professionals have used the surplus in each vial for an additional sixth dose. Even in these cases, each vial still contains a small quantity of vaccine, which can be used to perform skin tests.

Taking advantage of this fact, we evaluated 55 health care professionals to determine nonirritant concentrations for skin testing with SARS-CoV-2 mRNA vaccine.

All participants were selected from a group of health care professionals being vaccinated with the Pfizer SARS-CoV-2 vaccine, as part of the Portuguese National Vaccination Plan. Participants were inoculated with the first dose of the vaccine, and if they remained asymptomatic for 30 minutes, they were considered eligible for skin testing. Participants were excluded if they took antihistamines or drugs with antihistamine properties in the 5 previous days. All participants signed an informed consent. Patients were questioned on their atopic history and, specifically, drug allergy. Additional information from their clinical files was added retrospectively.

Each person underwent skin prick and intradermal tests with the undiluted vaccine and with a dilution of 1/10 with saline. The tests were performed in accordance with the literature.[4] A positive control with histamine (10 mg/mL) and a negative control with saline, performed by the prick test, were also carried out. Readings were made after 15 and 30 minutes for every test.

Seventy-five percent of the patients were women, with an average age of 42 ± 12 years (between 23 and 67 years of age). Atopic history is detailed in Table I. None of the patients had a history suggestive of PEG allergy, or allergy to other vaccines. Three of the participants presented a history of anaphylaxis: one selective to indomethacin (with no previous evaluation by an allergologist, but with a very suggestive story), another to Pru p 3 (previously confirmed by an allergologist), and the last had IgE-mediated allergy to penicillin and nonsteroidal anti-inflammatory drug–induced asthma and urticaria (previously confirmed by an allergologist).

All the skin prick tests with histamine were positive (wheals between 4 × 4 mm and 9 × 8 mm). All negative control prick tests were negative with the exception of a patient with symptomatic dermographism (wheal of 5 × 5 mm).

In 53 patients (96%), the vaccine prick and intradermal tests were negative. One patient showed erythema without pruritus or increase in diameter of the intradermal wheal in both the undiluted and 1/10 dilution. Another participant, with symptomatic dermographism, showed a positive reaction to the skin prick and intradermal tests, including the skin prick test with saline.

No participant developed symptoms suggestive of an allergic reaction within 24 hours of the first inoculation.

In conclusion, skin prick testing and intradermal testing can be performed with the Pfizer-BioNtech SARS-CoV-2 vaccine with its undiluted form. An open question remains about the exact positive predictive value these tests may have. These findings cannot be generalized to other vaccine preparations and do not address delayed reactions or adverse effects.

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TABLE I. Atopic history of the participants

Atopic history	No. of patients (n = 55)
Allergic rhinitis confirmed by allergic testing	11
Nonallergic rhinitis confirmed by allergic testing	1
Rhinitis-like symptoms with no previous evaluation by allergology	6
Allergic asthma confirmed by allergic testing	10
Nonallergic asthma confirmed by allergic testing	1
Asthma-like symptoms with no previous evaluation by allergology	2
Food allergy confirmed by allergic testing	2*
Food allergy with no previous evaluation by allergology	0
Drug allergy confirmed by allergic testing	1†
Drug allergy with no previous evaluation by allergology	6‡

NSAID, Nonsteroidal anti-inflammatory drug.

*One case of anaphylaxis related to Pru p 3, and 1 case of oral allergy syndrome related to nuts.

†Urticaria with beta-lactam antibiotics, with positive skin tests and/or oral provocation tests and NSAID-induced asthma and urticaria.

‡Two cases of urticarial-like symptoms with amoxicillin, 1 case of urticarial-like symptoms with metoclopramide, 1 case of urticarial-like symptoms with oral acetylcysteine, 1 case of face angioedema with aspirin (tolerating other NSAIDs), and 1 case of anaphylaxis with indomethacin (consistent history on 2 separate occasions, tolerating other NSAIDs).

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