

Allergic Reactions After Administration of Pfizer-BioNTech COVID-19 Vaccine to Health Care Workers at a Tertiary Hospital

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Comirnaty is an mRNA-based COVID-19 vaccine manufactured by Pfizer-BioNTech. In a clinical trial of 43 548 participants, the vaccine conferred 95% protection against COVID-19, and no severe allergic reactions were reported [1].

COVID-19 vaccines are contraindicated in patients who have previously experienced a severe allergic reaction to any component of the vaccine or to the first dose. Based on experience with other vaccines, systemic allergic reactions would be expected within a range of 1-5 cases per million applications [2].

Clinically, drug hypersensitivity reactions (DHRs) are classified as immediate or nonimmediate/delayed depending on their time of onset. Immediate DHRs are induced by an IgE-mediated mechanism and occur within 1-6 hours after the last administration, while nonimmediate DHRs are associated with a T cell-dependent mechanism and occur at any time from 1 hour after the initial drug administration [3]. Systemic immediate DHRs can be classified by severity [4].

Our objective was to report the clinical characteristics and the results of an allergy assessment of all health care workers (HCWs) from our hospital referred by the occupational health department after a suggestive DHR [3] following administration of the first dose of Comirnaty during January 10-19, 2021. We retrospectively reviewed the clinical charts of the HCWs. A thorough allergy study was conducted, including a detailed clinical history and skin tests. We performed skin prick tests (SPTs) with Comirnaty using the leftovers from vaccine vials and with an excipient of the vaccine, namely, polyethylene glycol-2000 (PEG-2000) (Poly (ethylene glycol) BioUltra, 2000, SigmaAldrich), at different concentrations (0.16-160 mg/mL). PEG has been reported to induce hypersensitivity reactions in drugs containing this

excipient [5-6]. A basophil activation test (BAT) with PEG-2000 and Comirnaty was also performed in patient 1, who had experienced mild generalized urticaria after the second dose despite premedication. The study was approved by the ethics committee of our hospital (HULP- PI-4733).

A total of 8446 first doses of Comirnaty were administered; of these, 6393 (75.7%) were administered to females. The median (IQR) age was 36.7 (34-42.75) years. None had received a vaccine during the previous 7 days or had COVID-19 symptoms or acute febrile illness at the time.

Through a questionnaire completed before receiving their vaccination, 127 HCWs reported a history of allergic reactions to drugs, 40 to food allergens, 18 to aeroallergens, 11 to metals, 4 to latex, and 65 to unspecified allergens. None reported a history of allergic reactions to vaccines or to excipients such as PEG or other ethylene oxide derivatives. HCWs were asked to call or to send an email to the occupational health department in the event of an adverse reaction after administration of the vaccine. A total of 207 adverse drug reactions were reported to this department.

Eleven suspected allergic reactions (0.13%) were reported after the first dose of the vaccine and were referred to the allergy department for assessment (Supplementary Table 1). Nine (81.8%) were reported in females, and the median age was 39 (29.5-56.5) years. All were suspected cases of mild allergic reactions, 10 within the first 24 hours and 1 within 48 hours, and no severe allergic reactions were reported. Four patients were treated with systemic corticosteroids or H₁ antihistamines, and none required hospitalization.

SPTs performed in 9 patients yielded negative results. The BAT result was also negative in 1 patient. Ten HCWs (90.9%) received the second dose of Comirnaty, and no severe allergic reactions were reported. Five of these 10 HCWs received premedication with H₁ antihistamines, and 2 of the 5 individuals experienced milder cutaneous symptoms. Five HCWs did not receive premedication with H₁ antihistamines, and 3 of them presented milder cutaneous symptoms. One HCW could not receive the second dose due to an intercurrent medical condition.

The Centers for Disease Control and Prevention (CDC) reported allergic reactions after administration of the first dose of Pfizer-BioNTech COVID-19 vaccine in 1 893 360 persons [7]. They found 83 cases of nonanaphylactic allergic reactions with cutaneous or mild respiratory symptoms and 21 cases of anaphylaxis (11.1 per million doses). Seventeen of these patients (81%) with anaphylaxis had a previous history of allergic reactions. Blumenthal et al [8] observed that acute allergic reactions were reported by 1365 HCWs after 64 900 first doses (2.10% [95%CI, 1.99%-2.22%]). These were more frequent—but not significantly so—with the Moderna vaccine than with Pfizer-BioNTech (2.20% [95%CI, 2.06%-2.35%] vs 1.95% [95%CI, 1.79%-2.13%]; *P*=.03) [6]. With Comirnaty (*n*=25 929), the number of cases of anaphylaxis was low (7 confirmed cases, 2.47/10 000 vaccinations). In our series, we found no cases of anaphylaxis. However, we did find a higher incidence of mild allergic reactions (0.13% vs 0.0044%) than the CDC, although this represented a lower incidence of acute allergic reactions (0.11% vs 1.95%) than in the study by Blumenthal et al [8].

Immediate DHRs related to vaccine administration are frequently associated with the inactive components or by-products of the vaccine manufacturing process, such as egg or latex [9]. In the case of Comirnaty, the presence of excipients such as PEG-2000 has been considered a potential cause of immediate DHRs [5,6,9-11]. PEG-encapsulated nanomedicines have caused pseudoallergic reactions in experimental models [12]. In addition, after endocytosis, the mRNA-free PEG in lipid nanoparticles floating on the cell surface interacts with IgE antibodies that bind to the FcεR1 receptor on mast cells or basophils and can trigger immediate release of inflammatory mediators [12]. Although we cannot define the underlying mechanism of each reaction, it seems likely that non-IgE-mediated mechanisms are involved, as suggested elsewhere [13]. In these mild cases where an IgE-mediated reaction to PEG has been ruled out, premedication with H₁ antihistamines prior to the second dose could help to block non-IgE-mediated histamine release and may alleviate symptoms and improve tolerability.

It is important to carefully evaluate all possible allergic reactions to the vaccine to prevent the patient being unnecessarily denied access to it [10]. In addition, all vaccination centers should be prepared for the early diagnosis and treatment of allergic reactions related to COVID-19 vaccines [11].

In conclusion, no severe allergic reactions were observed in a large group of HCWs after administration of the first dose of Comirnaty. None of the patients who experienced mild allergic-like reactions were shown to be sensitized to Comirnaty or to its excipient, PEG-2000. Although we cannot definitively rule out the occurrence of IgE-mediated reactions, it appears that most reactions could have a non-IgE-mediated mechanism. Finally, SPTs with the vaccine and its excipients could be useful in the allergy work-up of hypersensitivity reactions to COVID-19 vaccines, although further studies will help clarify their real value.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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