

Use of antihistamines for COVID-19 vaccine recipients with risk of anaphylaxis

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Abstract

Allergic reactions to COVID-19 vaccine ranging from mild to severe have been reported in patients with a history of anaphylaxis. Currently, no guidelines are available regarding prevention of allergic reactions in patients with high-risk of anaphylaxis who plan on receiving the SARS-CoV-2 vaccine. In this case-series study, two patients with a history of anaphylaxis had taken antihistaminic drugs prior to their BNT162b2 vaccinations and experienced no major allergic reactions afterwards. The use of antihistamines prior to COVID-19 vaccination may have affected the outcome of the two subjects with history of anaphylaxis history. However, further studies are needed to evaluate efficacy, generalizability and safety of the approach presented in this case-series.

Keywords: vaccine · anaphylaxis · antihistamine · COVID-19

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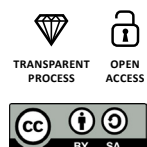
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Rapid development of vaccines for the coronavirus disease (COVID-19) and a worldwide implementation of vaccination programs have created an opportunity to slow down the pandemic. Currently there are over 100 million confirmed cases of COVID-19 and over 2.5 million deaths globally with several countries entering their third wave of the pandemic [1]. However, several safety issues were noted since the first days of inoculation [2], including reports of anaphylactic shock [2-3]. Observed hypersensitivity reactions resulted in restrictions in the vaccine qualification programs for people predisposed to anaphylaxis. The Medicines and Healthcare products Regulatory Agency (MHRA) and the Food and Drug Administration (FDA) currently disqualify from vaccination people with a history of anaphylactic shock to any of the ingredients contained in COVID-19 vaccines [4-6]. On the contrary, there are no contraindications to inoculation of people with no history of allergic reaction to BNT162b2, mRNA-1273 or ChAdOx1-S vaccine components or severe allergic reaction to the first dose of COVID-19 vaccines [7-8]. Since mRNA vaccines are novel products, the exact mechanism or the root cause of the allergic reaction associated with them is unknown [9]. However, polyethylene glycol (PEG), the inactive ingredient of BNT162b2 and mRNA-1273 vaccines (added for improved mRNA bioavailability) has been associated with anaphylaxis in the past and may be a cause in the recently reported anaphylactic reactions [9-12]. Our study examines the implementation of prophylactic doses of antihistaminic drugs for patients with high-risk of anaphylaxis undergoing COVID-19 vaccination. As of our knowledge, there are no current studies conducted on the prevention of anaphylactic responses from COVID-19 vaccines by the use of antihistaminic drugs.

Material and methods

We present two cases of medical professionals with history of severe allergic reactions, including anaphylactic shocks, caused by various factors. Both of them were vaccinated against COVID-19 by BNT162b2 while using an antihistamine drug as preventive measures. Consent to participate in the study was obtained as both subjects are also two co-authors of this paper.

Results

Case 1

A 39-year-old white male, a medical professional, was treated for hypertension with telmisartan (40 mg)

and hydrochlorothiazide (12.5 mg). He had a history of multiple severe allergic reactions, including anaphylactic reactions to three different stimuli. History of allergy events included an allergy to penicillin, generalized urticaria of unknown origin and computer tomography (CT) contrast allergy. Allergic reaction to penicillin was observed once during infancy, consisted of diffuse erythematous rash and dyspnea. There is no further data regarding this reaction and penicillin was never administered again.

The patient also reported recurrent generalized urticaria (since the age of 24) with intense itching and blisters up to 3-4 cm in diameter. It occurs once a week to once a month, as a reaction to an unknown trigger (apart from borderline reaction to wheat and rye flour no allergen was identified during routine testing) with tendency to aggravate by distress, physical activity, alcohol use or sleep deprivation. These reactions usually alleviate after the use of antihistaminics (20-40 mg of cetirizine or loratadine). Occasionally severe urticaria was accompanied by mild dyspnea and required administration of intramuscular or intravenous steroids in Emergency Departments. During a single episode of urticaria in 2009, dyspnea and hypotension were observed which resulted in intramuscular administration of adrenaline with a full recovery.

In 2018 this patient developed an anaphylactic shock after intravenous administration of a contrast agent (100 ml of iomeprolum 300 mg/ml) during a CT. Symptoms included generalized erythematous rash, dyspnea, hypotonia, weakness and confusion. The patient was immediately transported to the Emergency Department where he fully recovered after receiving 300 mg hydrocortisone, 2 mg clemastine and calcium intravenously.

Despite the history of allergic reactions, the patient was qualified for the BNT162b2 vaccination. On the day of the first dose of the vaccine he self-administered 20 mg loratadine (10 mg – 4h before, 10 mg – 2h before) and cetirizine (10 mg – 1h before) as a prophylaxis. Before the injection, his blood pressure was 140/90 mmHg. 15 min after the injection it dropped to 125/80 mmHg and the patient reported slight weakness and a rash limited to three itching lesions. Next, the patient took an additional dose of cetirizine (10 mg) resulting in full recovery. Apart from sedation and sleepiness which lasted for the next 24 hours and local pain in injection site, no additional adverse effects were noted.

Prior to receiving the second dose of the vaccine, the patient took similar prophylactic measures, although with a slightly increased dose (20 mg cetirizine 4 hours before the vaccination and additional 20 mg cetirizine 1 hour before). No local or generalized allergic reactions were observed after the second dose. Reported adverse effects were typical to BNT162b2 (muscle aches, fever for 1-2 days). No additional antiallergic agents were administered post-vaccination. One month follow-up revealed no long-term side-effects.

Case 2

A 54-year-old white male, medical professional with a history of a severe form of atopic dermatitis and a single episode of anaphylactic shock during the process of pollen desensitization. He reported that atopic dermatitis was diagnosed 8 years ago and it is now treated with 100 mg cyclosporine b.i.d. with increase in dosage to 150 mg b.i.d. for exacerbations, with additional use of mometasone and emollients locally. Allergies to several pollen (more severe to alder, birch, weeds, mugwort and cereals; mild to poplar and oak), mold and feline fur were noted since childhood. In 1996, attempts to desensitize to pollen were made but resulted in an anaphylactic reaction and were then discontinued. Symptoms included vertigo, confusion and hypertension. 500 mg hydrocortisone i.v. was administered and the patient recovered fully. Comorbidities included symptomatic epilepsy (probably due to arachnoid cyst) treated with levetiracetam 500 mg b.i.d. (no seizures for the last 7 years), bronchial asthma (only as a reaction to feline fur, not treated), hypertension (probably secondary to cyclosporine) treated with 5 mg amlodipine.

First and second doses of BNT162b2 were both preceded by administration of additional 5 mg desloratadine t.i.d. as prophylaxis. Regular treatment with usual doses of cyclosporine (100 mg b.i.d.) was continued. No allergic reactions were observed after either dose. Additional 5 mg desloratadine was administered a few hours after both inoculations. Adverse effects included only muscle aches, headache and general fatigue for half a day after the first dose of vaccination and muscle pain and mild fatigue after the second dose. Subject's blood pressure before and after vaccinations were within reference ranges. No additional anti-allergic agents were administered post vaccination. One month follow-up revealed no long-term side-effects.

Discussion

The two subjects in our case series both had a history of an anaphylactic reaction. A single center cohort study reported 19 patients who developed anaphylaxis to the COVID-19 vaccine. 31% of the 19 patients also had prior anaphylaxis but did not report using any prophylactic measures before their injections [13]. Anaphylactic response also appears to be more frequent among women. From December 14th to 23rd 2020, the Centers for Disease Control and Prevention (CDC) reported 21 patients (19 of them were female), who developed anaphylaxis from the BNT162b2 vaccine [2]. Similarly, the previously-mentioned single center study reported that 94% of their patients who developed anaphylaxis were females [13]. The subjects in our study were only males and had taken an antihistamine drug prior

to their two doses of the vaccination and successfully reported no major allergic reactions after their exposure to both doses of BNT162b2 vaccine. Despite the fact that the patients did not experience anaphylaxis after vaccination, we do not know how the two subjects would have responded if no antihistaminic drug was taken prior to it. However, the mild allergic reaction noted in Case 1 may suggest that the reaction experienced would have been more severe without medications. Currently the CDC does not recommend the use of antihistamines prior to COVID-19 vaccination because the prophylactic use may mask cutaneous symptoms, which could lead to a delay in the diagnosis and management of anaphylaxis. The decision on whether to administer antihistamines prior to vaccination should be made individually after assessing the risks and benefits of the patient. Large doses of antihistaminics were fairly safe in our cases, but further studies are needed to evaluate efficacy, generalizability and safety of this approach for people with anaphylaxis history.

Antihistamine agents remain the basis for prevention and treatment of allergies [14], but there are still no studies or guidelines regarding their use by people at risk of a severe allergic reaction from mRNA vaccinations. In regard to other vaccines, one case report found that the prophylactic use of loratadine along with prednisolone may have successfully prevented anaphylaxis to the subject who was injected with a purified chick embryo cell rabies vaccine (PCECV) [15]. However, additional studies on the prophylactic use of antihistamines for high-risk anaphylactic patients during any vaccination in general are limited.

Conclusions

The difficult access to the benefits of COVID-19 vaccination for people with a history of severe hypersensitivity reactions puts them at risk of coronavirus infection with all its possible complications. We believe that the steps towards fighting back against the pandemic by achieving herd immunity should be directed towards reduction of severe allergic reactions and decreasing the social hesitance to vaccinate.

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Conflicts of interest

The authors do not have an association that might pose a conflict of interest (e.g., pharmaceutical stock ownership, consultancy, advisory board membership, relevant patents, or research funding).

References

1. Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. *Lancet Infect Dis* [Internet]. 2020 May;20(5):533-4. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S1473309920301201>
2. Shimabukuro T, Nair N. Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Pfizer-BioNTech COVID-19 Vaccine. *JAMA* [Internet]. 2021 Feb 23;325(8):780. Available from: <https://jamanetwork.com/journals/jama/fullarticle/2775646>
3. Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Moderna COVID-19 Vaccine — United States, December 21, 2020 – January 10, 2021. *MMWR Morb Mortal Wkly Rep* [Internet]. 2021 Jan 29;70(4):125-9. Available from: http://www.cdc.gov/mmwr/volumes/70/wr/mm7004e1.htm?s_cid=mm7004e1_w
4. COVID-19: the green book, chapter 14a. Guidance [Internet]. UK Health Security Agency. 2022. Available from: <https://www.gov.uk/government/publications/covid-19-the-green-book-chapter-14a>
5. Moderna COVID-19 Vaccine [Internet]. FDA. 2022 [cited 2022 Jan 16]. Available from: <https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/moderna-covid-19-vaccine>
6. Comirnaty and Pfizer-BioNTech COVID-19 Vaccine [Internet]. FDA. 2022. Available from: <https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/comirnaty-and-pfizer-biontech-covid-19-vaccine#additional>
7. Sokolowska M, Eiwegger T, Ollert M, Torres MJ, Barber D, Del Giacco S, et al. EAACI statement on the diagnosis, management and prevention of severe allergic reactions to COVID-19 vaccines. *Allergy* [Internet]. 2021 Jun 15;76(6):1629-39. Available from: <https://onlinelibrary.wiley.com/doi/10.1111/all.14739>
8. Klimek L, Jutel M, Akdis CA, Bousquet J, Akdis M, Torres MJ, et al. ARIA-EAACI statement on severe allergic reactions to COVID-19 vaccines – An EAACI-ARIA Position Paper. *Allergy* [Internet]. 2021 Jun 15;76(6):1624-8. Available from: <https://onlinelibrary.wiley.com/doi/10.1111/all.14726>
9. Castells MC, Phillips EJ. Maintaining Safety with SARS-CoV-2 Vaccines. Longo DL, editor. *N Engl J Med* [Internet]. 2021 Feb 18;384(7):643-9. Available from: <http://www.nejm.org/doi/10.1056/NEJMra2035343>
10. Turner PJ, Ansotegui IJ, Campbell DE, Cardona V, Ebisawa M, El-Gamal Y, et al. COVID-19 vaccine-associated anaphylaxis: A statement of the World Allergy Organization Anaphylaxis Committee. *World Allergy Organ J* [Internet]. 2021 Feb;14(2):100517. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S1939455121000119>
11. Banerji A, Wickner PG, Saff R, Stone CA, Robinson LB, Long AA, et al. mRNA Vaccines to Prevent COVID-19 Disease and Reported Allergic Reactions: Current Evidence and Suggested Approach. *J Allergy Clin Immunol Pract* [Internet]. 2021 Apr;9(4):1423-37. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S2213219820314112>
12. Klimek L, Novak N, Cabanillas B, Jutel M, Bousquet J, Akdis CA. Allergenic components of the mRNA-1273 vaccine for COVID-19: Possible involvement of polyethylene glycol and IgG-mediated complement activation. *Allergy* [Internet]. 2021 Nov 17;76(11):3307-13. Available from: <https://onlinelibrary.wiley.com/doi/10.1111/all.14794>
13. Blumenthal KG, Robinson LB, Camargo CA, Shenoy ES, Banerji A, Landman AB, et al. Acute Allergic Reactions to mRNA COVID-19 Vaccines. *JAMA* [Internet]. 2021 Apr 20;325(15):1562. Available from: <https://jamanetwork.com/journals/jama/fullarticle/2777417>
14. Simon FER, Simons KJ. H1 Antihistamines: Current Status and Future Directions. *World Allergy Organ J* [Internet]. 2008;1(9):145-55. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S1939455119305915>
15. Tamma A, Jarvinen K, McCall B, Wong R, Sehu M. Satisfactory immune response following anaphylaxis to PCECV facilitated by the use of steroids and antihistamines. *Hum Vaccin Immunother* [Internet]. 2020 Jun 2;16(6):1441-3. Available from: <https://www.tandfonline.com/doi/full/10.1080/21645515.2019.16925624=2>