Research Letter

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Acute Allergic Reactions to mRNA COVID-19 Vaccines

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Anaphylaxis to the mRNA COVID-19 vaccines is currently estimated to occur in 2.5 to 11.1 cases per million doses, largely in individuals with a history of allergy.[1] Allergic concerns contribute to vaccine hesitancy; we investigated acute allergic reaction incidence after more than 60 000 mRNA COVID-19 vaccine administrations.

Methods

We prospectively studied Mass General Brigham (MGB) employees who received their first dose of an mRNA COVID-19 vaccine (12/16/2020-2/12/2021, with follow-up through 2/18/2021) (eMethods in the Supplement). For 3 days after vaccination, employees completed symptom surveys through a multipronged approach including email, text message, phone, and smartphone application links. Acute allergic reaction symptoms solicited included itching, rash, hives, swelling, and/or respiratory symptoms (eAppendix in the Supplement).

To identify anaphylaxis, allergists/immunologists reviewed the electronic health records of employees (1) reporting 2 or more allergy symptoms, (2) described as having an allergic reaction in MGB safety reports, (3) logged by the on-call MGB allergy/immunology team supporting employee vaccination, and (4) referred to MGB allergy/immunology. Episodes were scored using the Brighton Criteria[2] and the National Institute of Allergy and Infectious Diseases/Food Allergy and Anaphylaxis Network (NIAID/FAAN) criteria.[3] Confirmed anaphylaxis required meeting at least 1 of these 2 sets of criteria.

We described characteristics and outcomes of anaphylaxis cases. We calculated incidence rates and 95% CIs of self-reported acute allergic reactions and confirmed anaphylaxis, using vaccine administrations as the denominator. We compared

frequencies using χ^2 tests, considering a 2-sided *P* value of .05 statistically significant. Analyses were conducted in SAS version 9.4. This study was approved by the MGB Human Research Committee with a waiver of informed consent.

Results

Of 64 900 employees who received their first dose of a COVID-19 vaccine, 25 929 (40%) received the Pfizer-BioNTech vaccine and 38 971 (60%) received the Moderna vaccine. At least 1 symptom survey was completed by 52 805 (81%).

Acute allergic reactions were reported by 1365 employees overall (2.10% [95% CI, 1.99%-2.22%]), more frequently with the Moderna vaccine compared with Pfizer-BioNTech (2.20% [95% CI, 2.06%-2.35%] vs 1.95% [95% CI, 1.79%-2.13%]; *P* = .03, Table 1). Anaphylaxis was confirmed in 16 employees (0.025% [95% CI, 0.014%-0.040%]): 7 cases from the Pfizer-BioNTech vaccine (0.027% [95% CI, 0.011%-0.056%]) and 9 cases from the Moderna vaccine (0.023% [95% CI, 0.011%-0.044%]) (*P* = .76).

Individuals with anaphylaxis were a mean (SD) age of 41 (13) years, and 15 (94%) were female (Table 2); 10 (63%) had a prior allergy history and 5 (31%) had an anaphylaxis history. Mean time to anaphylaxis onset was 17 minutes (SD, 28; range, 1-120). One patient was admitted to intensive care, 9 (56%) received intramuscular epinephrine, and all recovered. Three employees, with prior anaphylaxis history, did not seek care.

Discussion

In this prospective cohort of health care employees, 98% did not have any symptoms of an allergic reaction after receiving an mRNA COVID-19 vaccine. The remaining 2% reported some allergic symptoms; however, severe reactions consistent with anaphylaxis occurred at a rate of 2.47 per 10 000 vaccinations. All individuals with anaphylaxis cases recovered without shock or endotracheal intubation.

The incidence rate of confirmed anaphylaxis in this study is larger than that reported by the Centers for Disease Control and Prevention based on passive spontaneous reporting methods (0.025-0.11/10 000 vaccinations).[1] However, the overall risk of anaphylaxis to an mRNA COVID-19 vaccine remains extremely low and largely comparable to other common health care exposures.[4] Although cases were clinically compatible with anaphylaxis, the mechanism of these reactions is unknown.

Most of the vaccine recipients with anaphylaxis had allergy histories, with 31% having prior anaphylaxis. However, given that approximately 5% of adults have severe food allergy histories[5] and 1% of adults have severe drug allergy histories,[6] this MGB employee cohort likely included almost 4000 individuals with severe food or medication allergy histories who were safely vaccinated.

Limitations of this study include the use of self-reported data. However, cohort participants were largely health care workers, and therefore self-report data reliability may be high. The use of vaccine administrations as the denominator for allergic

reaction incidence may have resulted in some inaccuracy. Although study methods might have missed cases of potential anaphylaxis, comprehensive prospective surveillance methods were used, and symptom survey alone captured 81% of all vaccinated employees. A northeastern US cohort may not be generalizable.

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Back to top

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