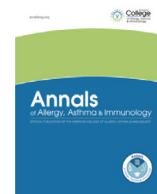




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Letters

Coronavirus disease 2019 vaccine skin testing and graded challenges in vaccine-hesitant patients

Vaccine hesitancy remains a significant obstacle to vaccine uptake.¹ Adverse reactions to coronavirus disease 2019 vaccines (CO19V), although rare,^{2,3} are a contributing factor. Studies^{4,5} report that many patients who fulfill the criteria for anaphylaxis can receive the vaccine. However, overcoming this hesitancy continues to be an issue for many who refuse to receive the vaccine.

We conducted an retrospective chart review approved by an institutional review board evaluating skin testing (ST) and graded-dose challenges (GC) with CO19V Pfizer-BioNTech (BNT162b2), Moderna (mRNA-1273), and Johnson & Johnson (J&J) (Ad26) in 62 patients hesitant to receive a CO19V because of a history of severe allergy to a medication, multiple allergies to medications, previous adverse reactions to a vaccine including CO19V, or a combination thereof.

In July 2021, with increased CO19V availability, 2 medical practices offered vaccine-hesitant patients the option of CO19V ST and GC. A ST was performed as percutaneous (1:1) and intradermal (1:100 and 1:10 dilution) followed by GC of 10%, 30%, and 60% doses, every 30 minutes. Patients were classified as “vaccine-complete (VC)” when they received a full dose and “vaccine-incomplete (VI)” when they did not receive a full dose regardless of symptoms experienced during ST or GC.

Data were collected and descriptive statistics were performed on demographics and reason for vaccination hesitancy, with the most cited being the following: (1) previous reaction to a CO19V (CO19V-prior-rxn) (31.7%) and (2) previous reaction to a non-CO19V (29.3%) or adverse drug reactions (non-CO19V-previous-rxn) (33%). Subanalysis was then performed on these 2 groups to determine whether patients who reacted to CO19V were less likely to complete vaccination.

In our study, a total of 62 patients (women = 56, men = 6) were evaluated with 56 ST and 55 GC performed; 50 of 62 (80.6%) patients received a full dose of a CO19V and, thus, classified as VC whereas 12 (19.4%) were VI. Overall, 18 (29%) patients were symptomatic during testing (ST or GC), 9 of whom were VC and 9 VI (Table 1). Of the 56 STs performed, 3 patients were ST-positive; 1 with a previous reaction to a CO19V, who was VC, and 2 with non-CO19V previous reactions who did not undergo GC. Of the 55 GC performed, 50 (90.9%) patients were VC, and 5 were VI (Table 1).

Among CO19V-prior-rxn patients (n = 25, 40.3%), 21 patients underwent ST (14 Pfizer, 1 Moderna, and 6 J&J) (Table 1). Only 1 of the 21 ST patients was ST-positive but VC. Of the 20 ST-negative patients, 16 patients were VC and 4 were VI. Of the 4 VI patients, 1 patient experienced chest tightness and pruritus during ST and

declined further testing, and 3 aborted GC because of symptoms experienced. All 4 non-skin-tested CO19V-prior-rxn patients were VC; these patients did not undergo ST as 3 were on antihistamines and 1 declined because of personal preferences.

We performed 24 GC on CO19V-prior-rxn patients (n = 25), 21 (87.5%) of whom were VC (Table 1); 1 patient declined GC because of chest tightness and pruritus during ST. The CO19V used during testing were: 16 Pfizer, 1 Moderna, and 7 J&J. A total of 4 out of the 21 VC patients reported subjective symptoms (generalized pruritus, oral pruritus, chest tightness, and facial pruritus). Of the 3 VI patients, that underwent GC, 3 were ST-negative but aborted GC because of symptoms experienced (chest tightness, dysphagia, face tingling, chest tightness). One ST-positive patient was VC and asymptomatic during ST and GC.

With respect to the type of CO19V previously received any type of vaccine received during testing, 11 of 13 (84.6%) patients with previous reaction to the Pfizer CO19V who underwent a GC were VC (8 Pfizer, 3 J&J), whereas 2 were VI (1 Pfizer, 1 J&J). Nine of 11 (81.8%) patients with a previous reaction to the Moderna CO19V who underwent a GC were VC (1 Moderna, 5 Pfizer, 3 J&J), whereas 2 were VI (2 Pfizer). One patient experienced previous reactions to both Moderna and J&J and successfully received a second J&J; this patient was included in the Moderna group.

Among non-CO19V-prior rxn patients (n = 37, 59.7%), 26 reported a history of drug allergies and 23 had reactions to other non-CO19V. A total of 33 of 35 (94.3%) patients were ST-negative (Table 1) and 2 were ST-positive. Of the 33 ST-negative patients, 27 (81.8%) were VC and 6 (18.2%) were VI. Of these 6 VI patients, 3 did not undergo GC because of symptoms experienced during ST (pruritus, cough, lip angioedema, facial flushing), 1 declined because of personal preferences, and 2 aborted GC because of symptoms experienced. The 2 non-skin-tested patients (1 on antihistamines, 1 negative histamine control) were also VC.

There were 29 of the 31 (93.5%) non-CO19V-prior-rxn patients who underwent a GC were VC (23 Pfizer, 6 J&J) (Table 1), 5 of whom reported subjective symptoms (tremulousness, oral/ear pruritus, cheek numbness, palmar pruritus, cough with postnasal drip) without objective findings. Of these 31 patients, 2 patients were VI and ST-negative, but aborted GC because of symptoms experienced (pruritus and flushing, tingling and anxiety).

To our knowledge, this is the largest report regarding the use of CO19V ST. Vaccine excipient ST exhibits low utility in predicting vaccine tolerance.^{6,7} Vaccine tolerance (80.6%) is high among all patients. Most patients (84%) who reported adverse reactions to a previous CO19V were VC, regardless of which CO19V they reacted to previously. Approximately 78% of patients with reactions to other

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Table 1
Demographics, Allergy History, Skin Testing, and Graded Challenge Results

Characteristic	Overall	CO19V-prior-rxn	non-CO19V-prior-rxn
Demographics			
Age, mean (SD)	47.0 (13.8)	46.6 (11.5)	46.2 (15.3)
Female sex (%)	56 (90.3)	24 (96)	32 (86.5)
Male sex (%)	6 (9.7)	1 (4)	5 (13.5)
Race (%)			
White	33 (53.2)	12 (48)	21 (56.8)
Asian	2 (3.2)	2 (8)	0 (0)
African American	5 (8.1)	1 (4)	4 (10.8)
Hispanic	2 (3.2)	1 (4)	1 (2.7)
Unknown	16 (25.8)	9 (36)	7 (18.9)
Mixed	4 (6.5)	0 (0)	4 (10.8)
Allergy history			
History of food, environmental or other allergies	33	15	18
History of reaction to other vaccines	25	2	23
History of drug allergies	42	16	26
History of anaphylaxis	24	10	14
Skin testing results			
Negative and vaccine-complete	43	16	27
Negative and vaccine-incomplete	10	4	6
Positive and vaccine-complete	1	1	0
Positive and vaccine-incomplete	2	0	2
No skin test performed and vaccine-complete	6	4	2
No skin test performed and vaccine-incomplete	0	0	0
Vaccine completion results			
Vaccine Complete	50	21	29
Vaccine Incomplete	12	4	8

Abbreviations: CO19V, coronavirus disease 2019 vaccine; CO19V-prior-rxn, previous reaction to a CO19V; non-CO19V-prior-rxn, previous reaction to a non-CO19V.

vaccines, reactions to drugs, or both were VC. Among patients who underwent GC (55), there was no statistical difference ($P = .64$, two-sided Fisher's exact test) in vaccine completion between those with a previous CO19V reaction (21/24 [87.5%]) or those with non-CO19V reactions (29/31 [93.5%]).

The limitations of this study include the small sample size, retrospective design, and reliance on patient recall of previous allergic reactions.

Our findings confirm that patients with previous adverse reactions to CO19V can receive future dosing suggesting “allergic reactions” reported by patients may be non-immunoglobulin E-mediated. A history of other drug reactions and prior non-CO19V reactions do not contraindicate CO19V. Offering CO19V ST and GC in an allergy office decreased vaccine hesitancy leading to the completion of vaccination series in most vaccine-hesitant patients.

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