

Single Dose Vaccination in Healthcare Workers Previously Infected with SARS-CoV-2

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Abstract: Coronavirus disease 2019 (COVID-19) vaccine shortages have led some experts and countries to consider untested dosing regimens. We studied antibody responses to a single dose of the Pfizer-BioNTech or Moderna vaccines in healthcare workers (HCW) with laboratory-confirmed COVID-19 infection and compared to them to antibody responses of HCW who were IgG negative to SARS-CoV-2 spike protein. HCW with prior COVID-19 showed clear secondary antibody responses to vaccination with IgG spike binding titers rapidly increasing by 7 days and peaking by days 10 and 14 post-vaccination. At all time points tested, HCW with prior COVID-19 infection showed statistically significant higher antibody titers of binding and functional antibody compared to HCW without prior COVID-19 infection ($p < .0001$ for each of the time points tested). In times of vaccine shortage, and until correlates of protection are identified, our findings preliminarily suggest the following strategy as more evidence-based: a) a single dose of vaccine for patients already having had laboratory-confirmed COVID-19; and b) patients who have had laboratory-confirmed COVID-19 can be placed lower on the vaccination priority list.

Although vaccination is a safe and effective method of prevention of coronavirus disease 2019 (COVID-19) [1], current shortages in vaccine production and distribution have led some experts and countries to consider untested regimens (one or half dose of a vaccine). Persons infected with COVID-19 are thought to have protective immunity and memory responses [2] for at least 6 months; however, neither recall responses nor ideal dosing has been studied in those previously infected with COVID-19. We compared antibody responses to COVID-19 vaccination in healthcare workers (HCW) with and without previous COVID-19 infection.

Methods

HCW who had previously enrolled in a hospital-wide serosurvey study [3], conducted from July to August, 2020 at the University of Maryland Medical Center were randomly contacted based on stratification into three groups: Group 1: IgG positive with history of symptomatic COVID-19; Group 2: IgG positive and with asymptomatic COVID-19; and Group 3: IgG antibody negative. Participants were vaccinated with either the Pfizer-BioNTech or Moderna vaccine, depending on personal preference and availability. Blood was drawn at Day 0 (or baseline), 7, 10, and 14 post-vaccination in December 2020, and January 2021, and plasma tested for IgG ELISA to spike trimer. The spike ELISA assay was modified from an assay we have previously published [4] to give a read-out of half-maximal binding titers, as well as end-point binding titers. Day 0 and 14 samples of vaccinees were also tested for SARS-CoV-2 neutralization by live virus neutralization, as previously published [5]. As controls, samples from inpatients and outpatients infected with COVID-19 were included, chosen at 1 and 2 months after onset of COVID-19 symptoms, when antibody titers would be at their peak.

Results

59 volunteers were enrolled (demographic details provided in Table 1). For the IgG ELISAs, at each of the Days 0, 7, 10, and 14 for ELISAs, COVID-antibody positive HCW (Group 2 and 3) had higher half-maximal and end-point IgG titers than Group 1 ($p < .0001$ for each by the two-tailed Mann Whitney test). At Days 0 and 14, Groups 2 and 3 had higher ID99 live virus neutralization titers than Group 1 ($p < .0001$ for each by the two-tailed Mann Whitney test). Figure 1 provides a summary of the above findings.

Discussion

We found that HCW previously infected with SARS-CoV-2, diagnosed via IgG to spike protein, had a classic secondary response to a single inoculation with a spike-based mRNA vaccine. That is, antibody titers started peaking at 7 days, and achieved higher titers and neutralization in 14 days compared to volunteers exposed to SARS-CoV-2 spike protein for the first time. Thus, there was a broad increase in binding and functional antibodies. This occurred for HCW who were both symptomatic and asymptomatic with their SARS-CoV-2 infection. Although we did not have peak titers for these individuals after natural infection, the titers developed after single vaccination was higher than peak titers in inpatients and outpatients with COVID-19, similar to what has been described in primary vaccination after 2 doses of the spike-based mRNA vaccines [6]. This secondary response occurs through activation of memory B cells [2]; and this study demonstrates recall responses through the antibody production stages in response to vaccination.

Given the above findings that one dose of vaccine can elicit a recall response, what we currently know about the duration of protective and memory responses, and until correlated of protection are identified, we think that in times of vaccine shortage, our findings preliminarily suggest the following strategy as more evidence-based: a) a single dose of vaccine for patients already having had laboratory-confirmed COVID-19; and b) patients who have had laboratory-confirmed COVID-19 can be placed lower on the vaccination priority list.

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Table 1. Study population baseline characteristics.

		Group 1	Group 2	Group 3	Inpatient	Outpatient
		(n=17)	(n=16)	(n=26)	(n=19)	(n=19)
Age (years)	Median	38	40	38	41	32
	Range	29-55	25-72	23-59	28-48	18 - 81
Gender [n (%)]	Male	5 (29)	4 (25)	3 (12)	16 (84)	8 (42)
	Female	12 (71)	12 (75)	23 (88)	3 (16)	11 (58)
Race/Ethnicity [n (%)]	African American	2 (12)	5 (31)	5 (19)	4 (22)	2 (11)
	Caucasian	12 (71)	9 (56)	18 (69)	1 (6)	13 (68)
	Asian	3 (18)	2 (13)	3 (14)	0 (0)	2 (11)
	Hispanic or Latino	0 (0)	0 (0)	0 (0)	13 (72)	2 (11)
Vaccine [n (%)]	Pfizer-BioNTech	10 (59)	6 (37)	13 (50)	N/A	N/A
	Moderna	7 (41)	10 (63)	13 (50)	N/A	N/A
Hospitalization [n (%)]		N/A	0 (0)	4 (15)	19 (100)	61 (94)
Days symptomatic	Median	N/A	0	10	N/A	N/A
	Range	N/A	0-2	3-34	N/A	N/A
Days from onset symptoms	Median	N/A	N/A	N/A	37	48
	Range	N/A	N/A	N/A	28-55	29-63

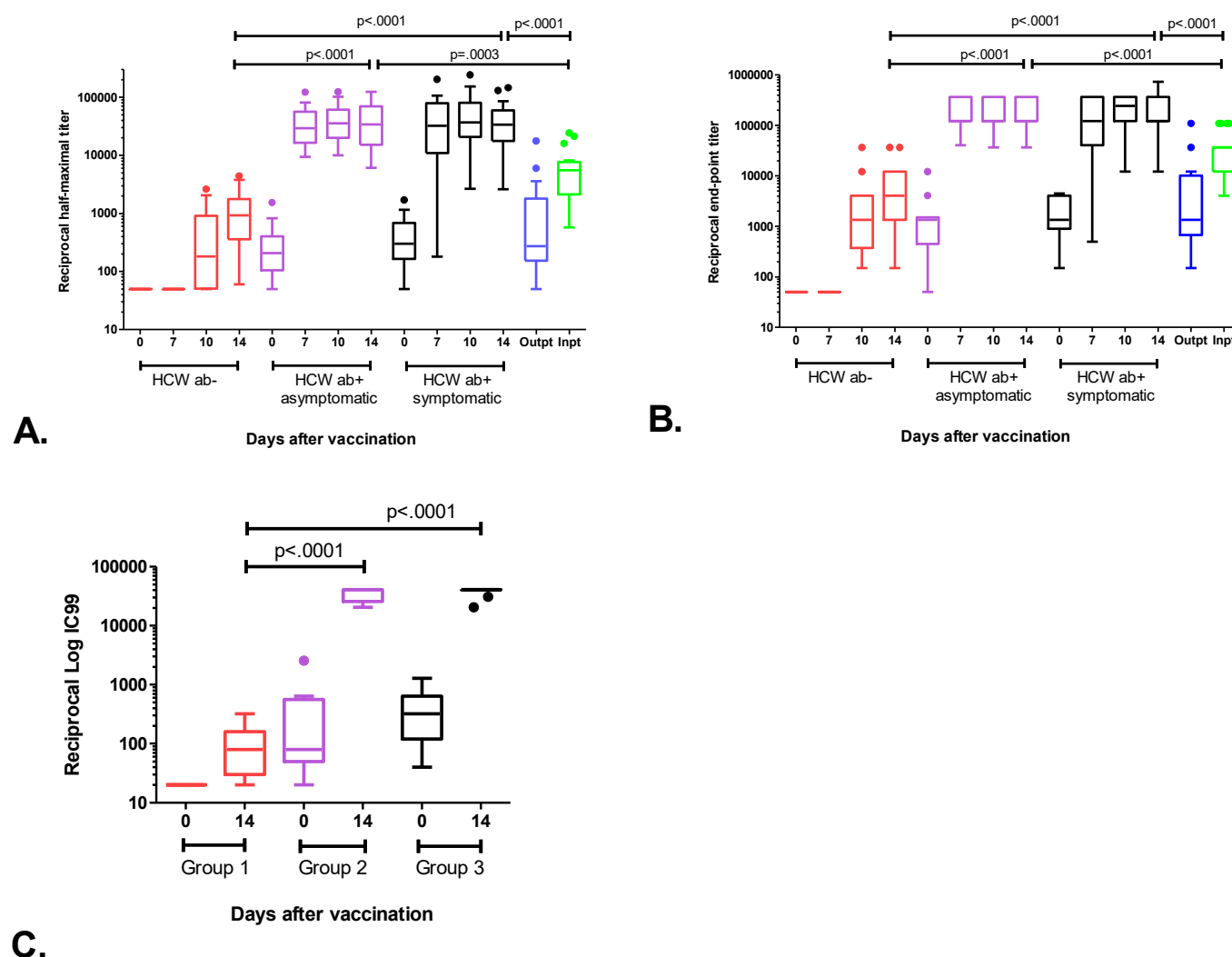


Figure 1. Anti-SARS-CoV-2 antibody responses after single dose of vaccination. After COVID-19 vaccination, plasma was drawn at 0, 7, 10, and 14 days and IgG binding titers against spike measured by ELISA and live virus neutralization at Day 0 and 14 measured. Single time point was also measured among COVID-19 outpatients or inpatients whose blood was drawn during peak antibody production (1-2 months after onset of symptoms). **A)** IgG spike trimer half-maximal titers. By 7 days and continuing to 14 days post vaccination HCW with prior COVID-19 who received a single vaccination developed higher peak IgG titers than HCW without COVID and COVID-19 infected patients. Half-maximal binding titers represent the dilution of plasma that achieves 50% of maximal binding of a known control that reaches saturation. **B)** IgG spike trimer end-point titers. By 7 days and continuing to 14 days post vaccination HCW with prior COVID-19 who received a single vaccination developed higher peak IgG titers than HCW without COVID and COVID-19 infected patients. End-point binding titers represent the highest dilution of plasma that that gives a reading above the statistically defined cutoff. **C)** Live virus neutralization. Serial dilutions of plasma was incubated for one hour with 100TCID₅₀ of WA-1 strain SARS-CoV-2. This admixture was added to Vero cells, and cytopathic effect was assayed using live/dead staining at 72 hours. At 14 days, HCW with prior COVID-19 who received a single vaccination developed higher neutralization titers than HCW without COVID. ID₉₉ defined as highest dilution at which 99% cells were protected. Group 1= SARS-CoV-2 IgG negative healthcare worker (HCW). Group 2= asymptomatic SARS-CoV-2 IgG positive HCW. Group 3= symptomatic SARS-CoV-2 IgG positive HCW. Box plots represent 25% to 75% percentile, with individual dots representing outliers using Tukey's method (1.5 x IQR).

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