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Antibody Responses 3-5 Months Post-Vaccination with mRNA-1273 or BNT163b2 in Nursing Home Residents

Nursing home residents in Ontario, Canada, were prioritized for vaccination with mRNA vaccines from Moderna (mRNA-1273) or Pfizer (BNT163b2) in December 2020-January 2021, which significantly reduced the high morbidity and mortality due to COVID-19.¹ Nursing home residents often fail to mount robust responses to vaccinations² and recent reports of breakthrough infections, particularly from variants of concern, raise questions about whether vaccination regimens elicit a sufficient humoral immune response or if booster doses are warranted.

Methods

We examined SARS-CoV-2 antibody levels and neutralizing capacity in nursing home residents 3-5 months after 2 doses of mRNA-1273 or BNT163b2 vaccination as per recommended schedules. Residents were recruited from 8 sites nursing homes in Ontario, Canada, between March and July 2021. Antibody levels and neutralization capacity from a previously published convalescent cohort were used as a comparator.³ All protocols were approved by the Hamilton Integrated Research Ethics Board, and informed consent was obtained.

Data are reported as a ratio of observed optical density to the determined assay cutoff optical density, with ratios above 1 considered positive. Neutralization capacity of these antibodies was assessed by cell culture assays with live SARS-CoV-2 virus, with data reported as geometric microneutralization titers at 50% (MNT₅₀), which ranged from below detection (MNT₅₀ = 10) to

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Data in this study were collected by the COVID-in-LTC Study Group. Members of the COVID-in-LTC Study Group include Jonathan L. Bramson, PhD; Eric D. Brown, PhD; Kevin Brown, PhD; David C. Bulir, MD, PhD; Judah A. Denburg, MD; George A. Heckman, MD, MSc; Michael P. Hillmer, PhD; John P. Hirdes, PhD; Aaron Jones, PhD; Mark Loeb, MD, MSc; Janet E. McElhaney, MD; Ishac Nazy, PhD; Nathan M. Stall, MD; Parminder Raina, PhD; Marek Smieja, MD, PhD; Kevin J. Stinson, PhD; Ahmad Von Schlegell; Arthur Sweetman, PhD; Chris Verschoor, PhD; Gerry Wright, PhD.

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MNT₅₀ = 1280.³ Antibody neutralization was measured against the wild-type strain of SARS-CoV-2 and the beta variant of concern (B.1.351). The beta variant was obtained through BEI Resources, National Institute of Allergy and Infectious Diseases, National Institutes of Health: SARS-Related Coronavirus 2, Isolate hCoV-19/South Africa/KRISP-K005325/2020, NR-54009, contributed by Alex Sigal and Tulio de Oliveira.

Differences between antibody levels and neutralization in individuals that received mRNA-1273 or BNT163b2 were assessed by chi-square of independence (proportions), Kruskal-Wallis test (median), and Student *t* test (mean). All statistical analyses were conducted using SAS, version 9.4 (SAS Institute Inc, Cary, NC).

Results

The majority of residents (97.1%) produced antibodies to the spike (S) protein post vaccination; however, fewer residents (87.68%) produced immunoglobulin G (IgG) to the receptor-binding domain (RBD) domain (Table 1). Residents who received mRNA-1273 had higher median levels of IgG S protein [mRNA-1273 = 2.9, interquartile range (IQR) 2.5-3.1] and IgG RBD (mRNA-1273 = 2.5, IQR 1.7-3.0) than those who received BNT163b2 (IgG Spike: BNT163b2 = 2.5, IQR 1.5-3.1, *P* = .015; IgG RBD: BNT163b2 = 1.5, IQR 0.7-2.6, *P* < .001). Participants who had been vaccinated with BNT163b2 had median values of both Ig Spike and RBD that were lower than the median values of a cohort of convalescent individuals. There were no differences between vaccine groups with respect to IgM/A to either S protein or RBD. No neutralizing antibodies were detected in ~20% of residents to the wild-type virus (30/155; 19%) or beta variant (27/134; 20%). Residents that received BNT163b2 had an ~4-fold reduction in neutralization to the wild-type strain and a ~2-fold reduction in neutralization to the beta variant relative to those who received mRNA-1273.

Discussion

Two doses of vaccine failed to elicit any antibody-mediated protective immunity in ~20% of nursing home residents. These data align with recent observations of decreased antibody production and/or neutralization after BNT162b2 vaccination in nursing home residents compared with healthy young individuals.⁴⁻⁶ In addition, we found that vaccination against SARS-CoV-2 with mRNA-1273 elicited a stronger humoral response compared with BNT162b2, with greater circulating IgG and neutralization antibody titers ~3 months after vaccination. The mRNA-1273 vaccine contains a higher dose of mRNA, which may imply that a higher dose is beneficial to generate protective immunity in nursing home residents.

Table 1
Antibody Levels and Virus Neutralization Capacity 60-130 Days Postvaccination in Nursing Home Residents

	Moderna (n = 77)	Pfizer (n = 61)	Total (N = 138)	P Value
Age, mean (SD)	84.53 (10.99)	80.77 (12.12)	82.87 (11.61)	.06
Sex, female (ref: male), n (%)	52 (67.53)	41 (67.21)	93 (67.39)	.97
Days between vaccine doses, mean (SD)	27.86 (0.35)	21.90 (1.26)	25.22 (3.09)	<.001***
Days between second dose and blood collection, mean (SD)	89.56 (12.80)	91.44 (17.70)	90.39 (15.13)	.49
IgG spike				
Median (IQR)	2.9 (2.5-3.1)	2.5 (1.5-3.1)	2.8 (2.1-3.1)	.015*
Below detection, n (%)	1 (1.30)	3 (4.92)	4 (2.90)	.32
IgG RBD				
Median (IQR)	2.5 (1.7-3.0)	1.5 (0.7-2.6)	2.2 (1.2-2.9)	<.001***
Below detection, n (%)	4 (5.19)	13 (21.31)	17 (12.32)	.004**
IgM spike				
Median (IQR)	0.3 (0.2-0.4)	0.2 (0.2-0.4)	0.3 (0.2-0.4)	.64
Below detection, n (%)	68 (88.31)	56 (91.80)	124 (89.86)	.50
IgM RBD				
Median (IQR)	0.1 (0.1-0.2)	0.2 (0.1-0.2)	0.1 (0.1-0.2)	.82
Below detection, n (%)	77 (100.00)	59 (96.72)	136 (98.55)	.19
IgA spike				
Median (IQR)	1.2 (0.7-1.9)	0.8 (0.5-1.4)	0.9 (0.6-1.8)	.032*
Below detection, n (%)	13 (16.88)	16 (26.23)	29 (21.01)	.18
IgA RBD				
Median (IQR)	0.3 (0.2-0.6)	0.3 (0.2-0.5)	0.3 (0.2-0.6)	.08
Below detection, n (%)	55 (71.43)	48 (78.69)	103 (74.64)	.33
MNT50 (wild-type)				
Median (IQR)	320.0 (80.0-640.0)	80.0 (40.0-320.0)	160.0 (40.0-640.0)	.002**
Below detection, n (%)	9 (11.69)	15 (24.59)	24 (17.39)	.047*
MNT50 (beta variant)				
n (n missing)	76 (1)	45 (16)	121 (17)	—
Median (IQR)	80.0 (40.0-80.0)	40.0 (40.0-80.0)	40.0 (40.0-80.0)	.019*
Below detection, n (%)	15 (19.74)	8 (17.78)	23 (19.01)	.79

IQR, interquartile range; RBD, receptor-binding domain.

*P < .05; **P < .01; ***P < .001.

Current mRNA SARS-CoV-2 vaccine regimens may not have equivalent efficacy in nursing home residents. Our findings imply that differences in the humoral immune response may contribute to breakthrough infections and suggest that consideration of the type of vaccine administered to older adults will have a positive impact on the generation of protective immunity.

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