Single dose of a mRNA SARS-CoV-2 vaccine is associated with lower nasopharyngeal viral load among nursing home residents with asymptomatic COVID-19

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ABSTRACT

In nursing home residents with asymptomatic COVID-19 diagnosed through twice-weekly surveillance testing, single dose BNT162b2 vaccination (Pfizer-BioNTech) was associated with -2.4 mean $\log_{10}$ lower nasopharyngeal viral load than detected in absence of vaccination (p=0.004). Since viral load is linked to transmission, single dose mRNA SARS-CoV-2 vaccination may help control outbreaks.

Keywords: SARS-CoV-2, COVID-19, Viral Load, Cycle Threshold, Asymptomatic

INTRODUCTION

Coronavirus disease 2019 (COVID-19) causes high mortality among nursing home residents [1]. Centers for Disease Control (CDC) guidelines recommend that nursing home residents be among the first vaccinated with one of two Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2) mRNA vaccines [2,3]. In a randomized, observer-blinded, placebo-controlled trial, the BNT162b2 mRNA SARS-CoV-2 vaccine (Pfizer-BioNTech) demonstrated 52% efficacy against symptomatic COVID-19 within the 21 days between first and second doses, and 95% efficacy ≥7 days after the second dose [3]. Given limited supplies of mRNA vaccines, some public health experts have advocated delaying second doses in favor of administering first doses to more people [4].

Individuals with asymptomatic COVID-19 account for up to 50% of all SARS-CoV-2 transmissions [5]. The viral load of the index case, rather than presence of symptoms, is the most important risk factor for transmission.[6] Viral load on hospital admission is also an independent predictor of mortality [7]. At present, the impact of a single dose of an mRNA SARS-CoV-2 vaccine on the development of asymptomatic disease or the viral load is unclear. In this study, we evaluated the effect of a single dose of the BNT162b2 vaccine on viral loads among individuals who developed asymptomatic COVID-19 while residing at a Veterans Affairs (VA) Community Living Center (CLC).

MATERIALS AND METHODS

VA Pittsburgh (Pennsylvania) CLC is a nursing home that houses approximately ~150 residents on 7 units, which are located on three floors. Subjects in this study had a negative baseline nasopharyngeal reverse transcription polymerase chain reaction test (RT-PCR, Palo Alto VA, CA) [8] for SARS-CoV-2 on 12/2/20. From 12/8/20-2/2/21, all residents underwent surveillance nares testing for SARS-CoV-2 with the BD Veritor antigen assay

(BD Life Sciences—Integrated Diagnostic Solutions, San Diego, CA) [9] every 2-5 days. The first positive result was confirmed with a nasopharyngeal BD Max SARS-CoV-2 RT-PCR test (BD Diagnostic Systems, Franklin Lakes, NJ, USA) [10].

Residents were screened daily for new or worsening cough, shortness of breath, cold or flu-like symptoms, headache, loss of taste or loss of smell, diarrhea, nausea, or vomiting. After a diagnosis of COVID-19 was established, residents were screened thrice daily for symptoms as described above. Criteria for symptomatic COVID-19 were those of the BNT162b2 vaccine randomized control trial [3]. Co-morbid conditions associated with severe COVID-19 were based on CDC guidelines [https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html]. On 12/16/20, residents without a prior diagnosis of COVID-19 who agreed to immunization received the first dose of the BNT162b2 vaccine.

Study endpoints were RT-PCR cycle threshold (Ct) for SARS-CoV-2 and calculated viral load for CLC residents with asymptomatic COVID-19 diagnosed from 12/2/20 (date of negative baseline surveillance RT-PCR testing at the facility) through 1/6/21 (date of the second vaccine dose). The Ct values of nucleocapsid 1 targets were compared using two-tailed t-test. Log_{10} viral load was calculated as previously described for the nucleocapsid 1 target [11] using average RNase P (RP) of 10 samples rather than a standardized RP Ct value. Specifically: log_{10} viral load = (45-normalized N1 Ct)/$log_2 10$, where normalized N1 Ct value = N1 for that sample- (corresponding RP value for that sample – average RP value for 10 samples). Log_{10} viral loads were compared with two-tailed t test.

RESULTS

Ten VA Pittsburgh CLC residents were diagnosed with asymptomatic COVID-19 from 12/2/20 through 1/6/21, when second doses of the BNT162b2 vaccine were offered at the facility. No further cases of asymptomatic COVID-19 were diagnosed through 2/2/21. Five residents with asymptomatic COVID-19 received a first dose of the vaccine on 12/16/20, which was 12-15 days prior to detection of SARS-CoV-2 in nasopharyngeal samples. The five other residents with asymptomatic COVID-19 were unvaccinated prior to diagnosis. Dates and results of tests are shown in Figure 1A. Four persons in each group were ≥ 65 years of age. All 10 persons had at least one co-morbid condition that predisposed to severe COVID-19 (Supplementary Table 1).

Median Ct values among unvaccinated and vaccinated residents with asymptomatic COVID-19 were 12.8 (interquartile range, 12.4-14.9) and 19.4 (interquartile range, 18.9-25.5), respectively (p= 0.009; Figure 1B). Mean $\log_{10}$ viral load was significantly higher in unvaccinated residents (9.5 (95% CI, 9.3 to 9.8)) than in vaccinated residents (7.1 (95% CI, 5.4 to 8.8)), respectively (p = 0.004; Figure 1C). Therefore, the viral load was -2.4 mean $\log_{10}$ lower among the vaccinated cohort.

DISCUSSION

In this small, single-center retrospective study of nursing home residents who had asymptomatic COVID-19 detected through twice-weekly surveillance testing, receipt of a single dose of the BNT162b2 vaccine within the previous 3 weeks was associated with a significantly lower nasopharyngeal viral load (-2.4 mean $\log_{10}$) than was detected in the absence of vaccination. There was greater inter-subject variability in SARS-CoV-2 viral loads among residents who were vaccinated than among those who were not vaccinated, likely reflecting divergent immune responses in an elderly and debilitated population [12].

Nevertheless, ranges of viral loads observed in vaccinated and un-vaccinated groups did not overlap, attesting to the strength of the observation. The clinical significance of our findings is unclear. However, the results are important since single dose mRNA vaccination, in which second doses are delayed beyond the 21-28 days studied in initial clinical trials, has been advocated as a strategy for protecting more members of the population in times of vaccine shortage [4]. The SARS-CoV-2 viral load is a critical factor in transmission [6], and lower nasopharyngeal burdens may result in quicker clearance of viremia [11]. Interventions that achieve a 90% reduction in SARS-CoV-2 production at time of hospital admission are predicted to shorten time to viral clearance by ~3 days and reduce mortality from 19% to 14% among individuals ≥65 years of age with risk factors [7]. Therefore, our study suggests that a mRNA SARS-CoV-2 vaccine may have an immediate impact on reducing the spread of SARS-CoV-2 among high-risk nursing home residents after a first dose, and that single-dose strategies may be viable public health approaches [4]. Larger follow-up studies are needed to test these hypotheses.

A notable strength of the study was our systematic surveillance testing and review of symptoms among nursing home residents. At the same time, the study has several limitations, beginning with its small sample size. The use of Ct value as a proxy for nasopharyngeal viral loads is an approximation with the potential for confounding. An antigen test was used to screen for SARS-CoV-2. As such, residents who had higher viral loads were most likely to be identified [9], and some asymptomatic cases with lower viral loads may not have been detected. Unrecognized cases of COVID-19 prior to 12/2/20 were not excluded by serologic testing; it is conceivable that such cases could have impacted viral loads during the study period. Three asymptomatic infections were detected after 12/2/20 but before the facility vaccination date of 12/16/20 (Figure 1). Viral loads were similar before and after 12/16/20, but it is possible that these data were affected temporally by factors such

as unrecognized transmission within the facility. Multiple providers obtained nares and nasopharyngeal samples, which could have led to sampling error. Finally, the study was underpowered to determine the impact of the BNT162b2 vaccine on acquisition of asymptomatic COVID-19 infection. The randomized, controlled trial that led to the Food and Drug Administration issuing an emergency use authorization for the vaccine did not determine the impact on development of asymptomatic COVID-19 [3].

In conclusion, vaccination with a single dose BNT162b2 was associated with lower SARS-CoV-2 viral loads than were detected in the absence of vaccination among nursing home residents with asymptomatic COVID-19. Therefore, a single dose of a mRNA SARS-CoV-2 vaccine may be effective at reducing viral transmission and outbreaks in nursing home settings.

Conflicts of interest.

Dr. Clancy has been awarded investigator-initiated research grants from Astellas, Merck, Melinta, and Cidara for studies unrelated to this project, served on advisory boards or consulted for Astellas, Merck, the Medicines Company, Cidara, Scynexis, Shionogi, Qpex and Needham & Company, and spoken at symposia sponsored by Merck and T2Biosystems. The other authors report no conflicts.

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FIGURES:

Figure 1A. SARS-CoV-2 Antigen Testing Over Time. Timelines are presented for 10 individuals who were residents at VA Pittsburgh CLC (y-axis). Dates of antigen testing are indicated on the x-axis. Individuals with circle and square symbols were in vaccinated and unvaccinated groups, respectively. Unfilled symbols indicated a negative test result. Solid black symbols indicate a positive test for SARS-CoV-2. Numbers to the right of the last symbol for each individual indicate the mean $\log_{10}$ nasopharyngeal viral load on the positive test date. The black arrow indicates the vaccination date of 12/16/20.

Figure 1B. Comparison of the cycle threshold values of SARS-CoV-2 among unvaccinated and vaccinated individuals, $p = 0.009$. Midlines indicate the median, boxes indicate interquartile ranges, whiskers indicate the upper and lower adjacent values (within 1.5-fold of the interquartile range).

Figure 1C. Comparison of the nasopharyngeal $\log_{10}$ viral loads of SARS-CoV-2 among unvaccinated and vaccinated individuals, $p = 0.004$. Midlines indicate the median, boxes indicate interquartile ranges, whiskers indicate the upper and lower adjacent values (within 1.5-fold of the interquartile range).

Figure 1A.

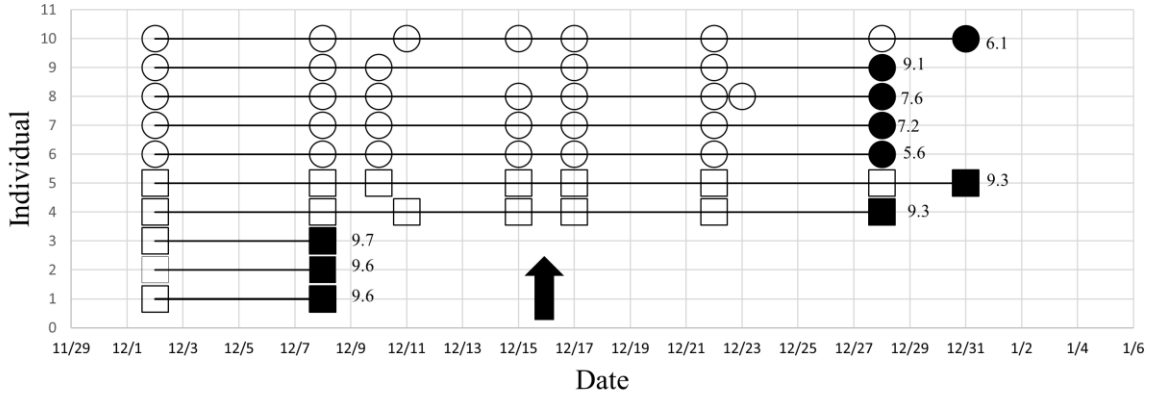

Figure 1B.

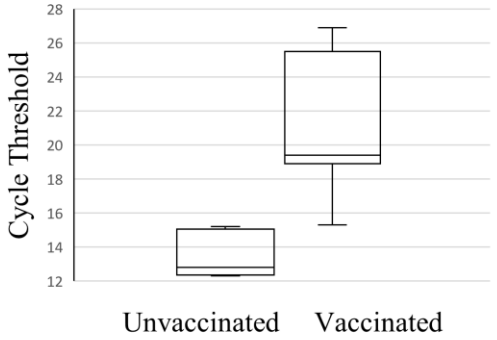

Figure 1C.