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Short communication

Is the second dose of vaccination useful in previously SARS-CoV-2-infected healthcare workers?

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ABSTRACT

Vaccines are the most important public health measure to protect people from COVID-19 worldwide. In addition, healthcare workers account for a large number of infected people. Protecting this population from COVID-19 seems crucial to preserve healthcare systems. In a context of few doses available, serological assays could be useful to decide whether one or two doses are needed. Our results show that a first dose of BNT162b2 mRNA vaccine seems to act as a boost after SARS-CoV-2 infection in healthcare workers with a previous SARS-CoV-2 infection; a second dose might therefore not be required.

1. Introduction

Since early 2020, the new and emergent coronavirus (SARS-CoV-2) spreads all over the world resulting in a pandemic. While some countries have been able to contain the epidemic with a combination of public health measures (extensive testing followed by isolation and tracing of contacts, near-universal masking, and target quarantines), most countries have failed to stop the epidemic. Much hope now resides in the potential of SARS-CoV-2 vaccines to reduce the risk of disease and infection. Implemented strategies aimed to maximize the early impact of vaccination in a context of few doses available [1]. As early as January 2021, a large vaccination campaign started in France first for populations at risk of severe COVID-19 but also rapidly for healthcare workers (HCWs) aged over 50 years or with underlying diseases, and then for all voluntary HCWs. Indeed, numerous studies underlined the risk of nosocomial transmission to and from HCWs in hospital settings [2,3].

Vaccination of patients and HCWs with a history of recent or late SARS-CoV-2 infection has become a major issue to reduce this risk. For these populations, current French guidelines recommend vaccination with only one dose for people who have recovered from COVID-19 at least 6 months before [4]. Moreover, serological assays are not included in the decision-making strategy of vaccination.

We aimed to provide data on the immune response induced by SARS-CoV-2 vaccines in real world context that can support this choice. Here, we reported kinetics of production of antibodies directed to the Spike protein of SARS-CoV-2 after a first and then a second dose of vaccine (conventional prime-boost strategy recommended) in HCWs.

2. Material and methods

All HCWs currently working at the Groupe Hospitalier Paris Saint-Joseph (Paris, France) and eligible to vaccination were proposed to be included in an observational cohort study after receiving the first and then second dose of the BNT162b2 mRNA COVID-19 vaccine (Pfizer/BioNTech, Mainz, Germany).

They were divided into two groups: HCWs with a previous history of SARS-CoV-2 infection [COVID-19 (+)] and HCWs with no history of SARS-CoV-2 infection [COVID-19 (-)] according to the RT-PCR and/or serology results to confirm previous contact with SARS-CoV-2. Minimal information was collected such as sex, age, dates of first and second vaccine doses.

HCWs had a first serological test performed 28 days after the first dose and before the second dose, and a second serological test was performed 21 to 28 days after the second dose.

HCWs with a history of COVID-19 came from the ongoing PERSOCOVID longitudinal observational cohort study. Briefly, these

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colleagues have been benefiting from a longitudinal serological follow-up since disease onset. For each of them, the level of antibodies directed to the Spike protein before vaccination was known. No HCW recently diagnosed with COVID-19 in the last 3 months were included in the study, according to French health agencies recommendations.

Serological assays used the quantitative test (SARS-CoV-2 IgG II Quant, Architect System, Abbott) for detecting serum antibodies directed to receptor-binding domain (RBD) of the Spike-1 protein of SARS-CoV-2. Quantitative results are converted in AU/ml. Dilution was performed for each result beyond 40,000 AU/ml according to the manufacturer's instructions. The positivity threshold was 50 AU/ml according to the manufacturer's instructions.

For statistical comparison, a Shapiro-Wilk test for normality of distribution was first performed and Student's *t*-test was performed for continuous variables, using the R software version 3.1.3 [4]. Significance was considered if $p < 0.05$.

All procedures were in accordance with the 1964 Helsinki declaration and its later amendments. According to French Health Public Law (CSP Article L1121-1), this study obtained approval from the local ethic committee.

3. Results

Seventy-three HCWs gave consent to participate in this study: 29 (39.7%) COVID-19(+) HCWs and 44 (60.3%) COVID-19(-) HCWs. No case of severe COVID-19 was recruited in this study and median [IQR] age of included HCWs was 43.5 [34–56.5] years old. The median time from first dose to serology was 25 days and 28 days from second dose to second serology.

We first reported a significant difference in anti-Spike antibody levels (median [IQR]) around 46-fold higher in COVID-19(+) HCWs [28,111 (15,032–33,967) AU/ml] than COVID-19(-) HCWs [642 (338–1,170) AU/ml] ($p < 0.001$) after the first dose. Antibody levels produced after the first dose in COVID-19(-) HCWs are quite similar than those observed in COVID-19(+) HCWs (324 [116–630] AU/ml) not yet vaccinated. In the latter, antibody levels increased on average by 88-fold after the first vaccine dose (Fig. 1).

After the first vaccine dose, COVID-19(-) HCWs presented a median level of IgG anti-Spike of 617 [338–1,147] AU/ml and their median level significantly increased 28 days after their second dose at 9,711 [4,978–15,473] AU/ml ($p < 0.001$). Previous infection seemed to be analogous to natural immune priming.

After the second dose, antibody levels of COVID-19(-) HCWs significantly increased [10,491 (5,341–16,193) AU/ml] without reaching the levels usually observed in COVID-19(+) HCWs after a single dose. For COVID-19(+) HCWs, we observed that the second dose did not significantly increase antibody levels [35,459 (11,565–38,500) AU/ml; $p = 0.18$] (Fig. 1).

4. Discussion

Following a single dose of BNT162b2, HCWs with a previous history of SARS-CoV-2 infection had a significantly higher antibody response than naive HCWs. The first dose of the vaccine seems to act as a boost after SARS-CoV-2 infection and a second dose might not be required in case of previous SARS-CoV-2 infection.

A delayed booster beyond the 30 days initially recommended for the BNT162b2/Pfizer vaccine could then be proposed. This is important to accelerate vaccine rollout in a context of few doses available [1].

Furthermore, COVID-19 is associated with an increase in HCWs absenteeism making the management of a public health crisis even more complicated [5].

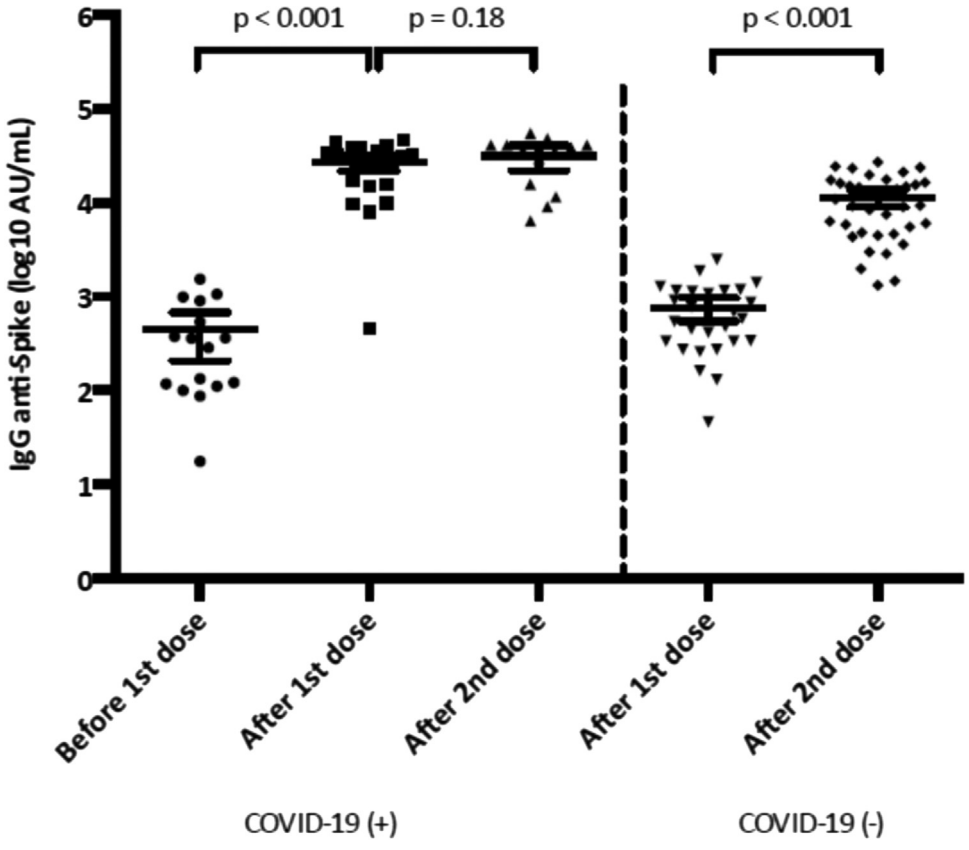

Fig. 1. Evolution of anti-Spike IgG titer expressed in log10 AU/ml during the vaccination protocol, according to history of COVID-19.

However, we also reported a paradoxically lower response than expected in one COVID-19(+) HCW. This HCW presented a positive RT-PCR and a positive serological assay confirming previous contact with SARS-CoV-2. This suggests that the use of serological tests could be useful to confirm adequate vaccine response without however the correlate of protection value. In case of immunosuppression, a third dose of vaccine may be recommended [6,7]. Finally, in other vaccine strategies, serology is recommended to monitor vaccine efficacy in immunocompromised patients [8]. Indeed, here no neutralization assays were performed because they are difficult to set up on a routine basis [9]. Manisty *et al.* showed that antibody levels after the first injection in naive individuals were comparable to pre-vaccination levels in previously infected individuals [10]. Our study showed that the levels after the first and second dose in previously infected HCWs are not significantly different. This would confirm the lack of benefit of a second dose in this population. For HCWs with a previous SARS-CoV-2 infection, determination of antibody levels produced after the first dose can be proposed just before the second dose to decide whether it is necessary.

Kinetics of natural anti-Spike antibody levels decrease more or less rapidly according to the initial level of IgG produced. In some cases, anti-Spike antibodies become undetectable beyond 6 or 8 months [11,12]. This also raises the question of the durability of the antibodies produced either after prime or boosted vaccination as well as for COVID-19 episode, and the impact of high initial antibody levels.

Our study provides additional information on the positioning and usefulness of serological tests in the COVID-19 vaccine strategy to maximize coverage and impact.

Human and animal rights

The authors declare that the work described has been carried out in accordance with the Declaration of Helsinki of the World Medical Association revised in 2013 for experiments involving humans as well as in accordance with the EU Directive 2010/63/EU for animal experiments.

Informed consent and patient details

The authors declare that this report does not contain any personal information that could lead to the identification of the patient(s) and/or volunteers.

Disclosure of interest

The authors declare that they have no competing interest.

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