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Letter to the editor

Anti-SARS-CoV-2 IgG antibodies in patients with or without SARS-CoV-2 infection after BNT162b2 vaccine booster

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1. Introduction

Universal coronavirus disease 2019 (COVID-19) vaccination is now considered the most effective strategy to mitigate the unfavourable clinical and organizational consequences of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections, even within healthcare environments [1]. Recent evidence reinforces the concept that vaccinations against SARS-CoV-2 is effective to limit the burden of healthcare-associated COVID-19 outbreaks [2]. Nonetheless, since it may be supposed that overlapping SARS-CoV-2 infections occurring after administration of vaccine booster doses may contribute to provide a further amplifying stimulus to the humoral response, we investigated the effect of post-booster SARS-CoV-2 infections on anti-SARS-CoV-2 antibodies elicited by a BNT162b2 vaccine booster in a cohort of baseline SARS-CoV-2-seronegative healthcare workers.

2. Materials and methods

The main characteristics of this retrospective observational SARS-CoV-2 serosurveillance study have been described elsewhere [3]. Briefly, the anti-SARS-CoV-2 spike trimeric IgG were measured with DiaSorin Trimeric spike IgG immunoassay on Liaison XL (DiaSorin, Saluggia, Italy) [4] in healthcare workers undergoing primary vaccination with Pfizer/BioNTech BNT162b2 (Pfizer Inc., New York, US; two 30 µg doses, with 3-week interval) followed by administration of homologous vaccine booster (30 µg single-dose) more than 8 months later. Molecular testing for detecting symptomatic and asymptomatic SARS-CoV-2 infections (Seegene Allplex SARS-CoV-2 Assay; Seegene Inc., South Korea or Altona Diagnostics RealStar SARS-CoV-2 RT-PCR Kit; Altona Diagnostics GmbH, Hamburg, Germany) was conducted at 2–4 weeks intervals by nasopharyngeal swab, throughout the study. Venous blood samples were drawn before either dose of primary vaccination, at 1, 3 and 6 months afterwards and, finally, before and 1 month after receiving the homologous vaccine booster dose. Statistical significance (set at $p < 0.05$) of differences in serum anti-SARS-CoV-2 spike trimeric IgG values, expressed as kilo Binding Antibodies Units per litre (kBAU/L), was assessed with Mann-Whitney test, using Analyse-it (Analyse-it Software Ltd, Leeds, UK). Written informed consent for vaccination and participation to the serosurveillance study was obtained from all participants. This observational retrospective study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Verona and Rovigo Provinces (59COVIDCESC; November 3, 2021).

3. Results

The final study population consisted of 67 baseline seronegative (i.e. pre-vaccination) healthcare workers, 14 with (median age, 42 years; IQR, 31–48 years; 29% of females) or 53 without (median age, 46 years; IQR, 34–54 years, 60% of females) a diagnosis of SARS-CoV-2 infection within 4 weeks after receiving the homologous booster vaccine dose. The variation of anti-SARS-CoV-2 spike trimeric IgG in both cohorts is shown in Fig. 1. No significant difference in serum concentration of anti-SARS-CoV-2 spike trimeric IgG levels was observed throughout the study period (all $p > 0.05$) between subjects with or without a diagnosis of post-booster SARS-CoV-2 infection. Although the median levels of anti-SARS-CoV-2 spike trimeric IgG at 1 month after receiving the booster vaccine dose appeared slightly higher in subjects with

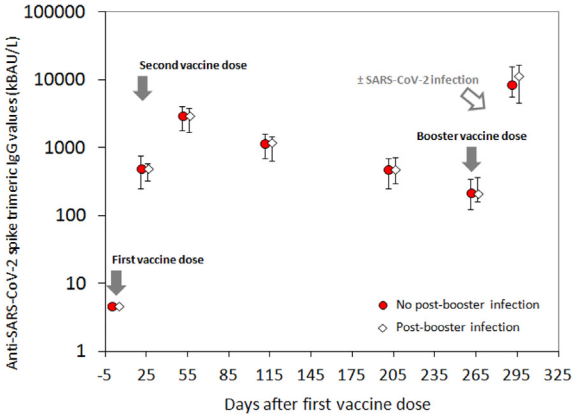

Fig. 1. Kinetics of serum anti-SARS-CoV-2 spike trimeric RBD IgG antibodies in baseline seronegative recipients of BNT162b2 mRNA-based primary vaccination and booster with or without post-booster SARS-CoV-2 infection. Results are shown as median and interquartile range (IQR).

Abbreviations: COVID-19, coronavirus disease 2019
SARS-CoV-2, severe acute respiratory syndrome coronavirus 2
Ig, Immunoglobulin

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post-booster SARS-CoV-2 infection (11,720 kBAU/L; IQR, 4,543–16,775 kBAU/L) than in those without (8,700 kBAU/L; IQR, 5,463–15,733 kBAU/L), this difference was not statistically significant (p = 0.257). The rate of subjects with protective values (i.e., >264 kBAU/L, corresponding to the 80% limit of COVID-19 vaccine efficacy against symptomatic disease as estimated by Feng et al. [5]) was 100% in both cohorts after booster vaccine dose.

4. Conclusion

The results of this study provide evidence that the short-term humoral response to COVID-19 vaccine booster may be comparable between healthcare workers with or without a diagnosis of post-booster SARS-CoV-2 infection. This aspect suggests that the anti-SARS-CoV-2 humoral response, at least with respect to quantitative antibody levels, may not be proportional to COVID-19 vaccine dosage or to the trigger of an overlapping SARS-CoV-2 infection in vaccinated people. Although the impact of different SARS-CoV-2 lineages on pre-existing immune memory may not be homogenous, it seems reasonable to conclude that booster vaccine doses may not substantially enhance antibody titers in people with recent SARS-CoV-2 infections, whilst a recent infection may instead confer major protection against currenly epidemic viral lineages.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the 1964 Helsinki declaration and its later amendments. The study was approved by the Ethics Committee of Verona and Rovigo Provinces (59COVIDCESC; November 3, 2021).

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None.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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