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Research Note

SARS-CoV-2 vaccine humoral response in adults with Down syndrome

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ABSTRACT

Objective: People with Down syndrome (DS) are particularly vulnerable to coronavirus disease 2019 (COVID-19) and show altered immune response to vaccination. We aimed to evaluate the immune response of a group of adults with DS treated with standard regimens of SARS-CoV-2 vaccine as compared with an age- and sex-matched group of persons without DS.

Methods: We compared antibody responses between 42 subjects with DS (41.6 ± 10.8 years, 57% male), and an age- and sex-matched comparison group of healthy health care workers (HCW) (41.4 ± 8.8 years, 54.8% male) after SARS-CoV-2 vaccination with the standard regimen of BNT162b2 mRNA COVID-19. Receptor binding domain (RBD) IgG antibodies were assessed at 4 time points (baseline, 21 days after the first dose, 21 days after the second dose, and 6 months after the first dose) with Siemens SARS-CoV-2 IgG (COV2G) antibody test.

Results: We observed significantly different antibody responses at all time points after vaccination (HCW vs. DS: 7.9 ± 3.9 vs. 1.4 ± 3.6 IU/mL at 21 days after first dose; 358.5 ± 3.8 vs. 38.1 ± 3.0 IU/mL at 21 days after second dose; 34.6 ± 2.4 vs. 7.9 ± 3.1 IU/mL at 6 months after vaccination) and a significantly different time course of decline in antibody titers between the two groups.

Discussion: Subjects with DS have a valid antibody response to SARS-CoV-2 vaccination. However, this response is lower than that of subjects in the HCW group. This finding could indicate a more rapid decline in the protective effects of the vaccination in subjects with DS and could suggest that people with DS may benefit from a booster dose of vaccine. Michela Sali, Clin Microbiol Infect 2022;28:1155.e1–1155.e4

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Introduction

People with Down syndrome (DS) have shown a particular vulnerability when affected by COVID-19 and therefore in many countries they have been prioritized to receive anti-SARS-CoV-2 vaccination [1]. It is thought that the causes of this increased risk of adverse events in DS can be ascribed to the contribution of several factors, including the impaired inflammatory profile in DS [2], the not fully elucidated interactions between the SARS-CoV-2 genome and the genetic alterations of DS [3,4], and the inherent complexity of clinical management of these individuals [5,6]. Moreover, due to altered immune responses, introduction of additional booster doses is known to be required for other standard vaccines in people with DS [7]. Although available data so far indicate good efficacy, safety, and tolerability of SARS-CoV-2 vaccines in the general population, there is no data available on the effects in persons with DS.

We aimed to evaluate the immune response of a group of adults with DS treated with standard regimens of SARS-CoV-2
Methods

This prospective study took place in the Day Hospital of Health Care Continuity of Fondazione Policlinico Universitario A. Gemelli IRCCS between March and December 2021. We randomly selected adults with DS in clinical follow-up (FU) at the Day Hospital who received the SARS-CoV-2 vaccination. No particular inclusion criteria were applied except not having contracted COVID-19, being eligible for vaccination, and being willing to participate. Data were compared with those obtained from healthy health care workers (HCW) of our institution since January 2021 and meeting the same inclusion criteria. The two groups were matched for age and sex by the cardinality method provided by the Matchit package in R with the optimization performed by GLPK [8].

All participants received two doses of BNT162b2 mRNA COVID-19 vaccine (Comirnaty) 21 days apart and were assessed for the detection of receptor binding domain (RBD) IgG antibodies using Siemens SARS-CoV-2 IgG (COV2G) antibody tests [9], at 4 time points:

1. T0 – Baseline assessment at day 0 in the same morning before the first vaccine dose.
2. T1 – 1st FU visit at day 21, that is, 21 days after the first dose, in the same morning before the second vaccine dose.
3. T2 – 2nd FU visit at day 42, that is, 21 days after completing the vaccination schedule.
4. T3 – 3rd FU visit at day 180, that is, 6 months after the first dose.

Immune response was normalized according to World Health Organization standards [10] and expressed in international units (IU/mL). Besides the peripheral blood draw for antibody detection, a comprehensive medical assessment and a detailed history on possible SARS-CoV-2 exposure, contagion and clinical course were obtained at each visit.

Comparisons were performed with \( \chi^2 \) test for categorical variables. Because of their extreme scatter and skewness, antibody titres were analysed after logarithmic transformation. Results were presented as geometric mean and standard deviation factor. For each timepoint, comparisons of treatment effect were performed by \( t \)-test of the ratio of the logarithm of the antibody titre. A linear mixed-effects model for repeated measurements was used to study the time course of antibody responses in the two groups under study. Data were analysed with R v4.03.

Discussion

This study reports a first evidence of antibody response to SARS-CoV-2 vaccination in a sample of people with DS. A significant difference is seen both at time T2 and at time T3. Importantly, the DS group has appreciable responses even if evidently lower compared to the ones in the comparison group. However, the fact that antibody levels decline to a lower level could reflect the risk of no longer being protected by the effects of vaccination at an earlier time than the general population.

These findings appear to be in line with previous research highlighting an altered immune response against various microbial species and after vaccine administration [11]. A similar pattern of response resembles that observed also in other conditions of immunosuppression [12].

The study has several limitations as it assesses only the effect of a single type of vaccine, it compares two groups of subjects consisting of convenience samples, it only measured IgG titres and no other immunoglobulins, and most of all it lacks analyses of the cell-mediated immune response. Nonetheless, these preliminary results raise the question on how to properly manage large-scale vaccination in this vulnerable population.

While further research in the field is certainly recommended, we believe that in view of our findings, of the increased risk of
adverse events from COVID-19 in these individuals, and of the worryingly different accessibility to care these people received during the pandemic [13], it would be important to encourage their prioritization to receive a third booster dose.

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**Author’s contributions**

MS - conceptualization, methodology, validation, resources, data curation, writing review/editing, supervision; AC - conceptualization, methodology, software, formal analysis, data curation, writing original draft, visualization, supervision; ADP - investigation, data curation, project administration; MPB - investigation, data curation; GZ - conceptualization, methodology, supervision; MS - conceptualization, methodology, resources, supervision; FL - conceptualization, methodology, resources, supervision; GO - conceptualization, methodology, validation, resources, data curation, writing review/editing.

**Transparency declaration**

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**Appendix A. Supplementary data**

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cmi.2022.04.008.
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