Humoral Response to Third Dose of SARS-CoV-2 Vaccines in the CKD Spectrum

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Information on the effect of a third dose of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine in advanced CKD is incomplete (1). We assessed the humoral response up to 6 months after receipt of two or three doses of the SARS-CoV-2 vaccine across the CKD spectrum. SENCOVAC is a prospective, multicentric study of four cohorts of patients with CKD: kidney transplant, hemodialysis (HD), peritoneal dialysis (PD), and nondialysis CKD (eGFR <30 ml/min per 1.73 m²) (2,3). Patients were vaccinated against SARS-CoV-2 during routine clinical care. Some patients received a third dose of an mRNA vaccine. This depended on the timing of vaccination drives by local health authorities. We assessed anti-Spike antibodies (CLIA, Covid-19 Spike Quantitative Vircell IgG Montost; Vircell SL, Spain) kinetics at a prespecified 6-month time point after completing the original vaccination schedule (2,3). The study was approved by the ethics committee of Instituto de Investigación Sanitaria-Fundación Jiménez Díaz (IIS-FJD) (February 2021).

Antibody titers were assessed at 28 days in 1736 patients, 3 months in 1371 patients, and 6 months in 1008 patients. At 6 months, 175 (17%) were kidney transplant recipients, 64 (6%) were on PD, 698 (70%) were on HD, and 71 (7%) were patients with CKD. Patients had received two doses of BNT162b2 (Pfizer-BioNTech; 305, 30%) or mRNA-1273 (Moderna; 703, 70%). Additionally, 624 (65%) patients received a third dose (26% BNT162b2, 74% mRNA-1273): 118 (71%) kidney transplant recipients, 20 (37%) patients on PD, 451 (67%) patients on HD, and 35 (51%) patients with CKD. The third dose was given a median of 144 (111–170) days after the second dose (125 [85–156] days in kidney transplant recipients, 145 [125–183] days in patients on PD, 147 [115–174] days in patients on HD, and 148 [125–188] days in patients with CKD).

Six months after the initial vaccination schedule, anti-Spike titers were lower in kidney transplant recipients than in patients on HD (P<0.001) (Figure 1A). Similarly, among patients with negative baseline anti-Spike antibodies, kidney transplant recipients had lower anti-Spike antibodies titers at 6 months than patients on HD (P<0.001). Anti-Spike antibody titers were lower in patients on PD than in those on HD (P<0.001). At 6 months, patients who had received a third vaccine dose had higher anti-Spike antibody titers than those without the third dose (P<0.001) in all CKD cohorts. Among patients who did not receive a third dose, antibody titers decreased significantly from 3 to 6 months (P<0.001).

According to the manufacturer, a positive humoral response was defined as anti-Spike IgG titters >36 U/ml. A positive response at 6 months among those receiving versus not receiving a third dose, by CKD subgroup, was as follows: 94 of 118 (80%) versus 25 of 47 (53%): P=0.002 kidney transplant recipients, respectively; 20 of 20 (100%) versus 24 of 34 (71%): P=0.01 patients on PD, respectively; 432 of 451 (96%) versus 138 of 217 (64%): P<0.001 patients on HD, respectively; and 34 of 35 (97%) versus 24 of 33 (73%): P=0.02 patients with CKD, respectively (Figure 1B). These responses were higher than in patients without a third dose (P<0.001). Among patients without humoral response at 3 months, 72 (69%) seroconverted after the third dose. The percentage of seroconverted patients was numerically higher with a third dose of mRNA-1273 (58%) than of BNT162b2 (38%: P=0.07). Among the CKD cohorts, 36 of 58 (62%) kidney transplant recipients, 34 of 45 (76%) patients

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Figure 1. | Anti-Spike antibodies during follow-up in CKD cohorts. (A) Anti-Spike antibodies titers during follow-up in different CKD cohorts. Data show anti-Spike antibodies titers of all patients irrespective of their baseline anti-Spike antibody titers. (B) Presence of anti-Spike antibodies during follow-up in the different CKD cohorts. Data are expressed as the percentage of patients with the presence of anti-Spike antibodies (i.e., titer >36 IU/ml). The table shows the sample size of each CKD group across each time point. Only significant P values are shown. HD, hemodialysis; PD, peritoneal dialysis.
on HD, and two of two (100%) patients with CKD seroconverted after the third dose.

In an adjusted multivariable model using logistic regression, a positive humoral response at 6 months was associated with initial mRNA-1273 vaccine [hazard ratio [HR], 1.78; 95% confidence intervals [95% CI], 1.11 to 2.88; \(P = 0.02\)], a positive humoral response at 3 months (HR, 26.2; \(P < 0.001\)), receiving a third dose (HR, 22.9; 95% CI, 8.06 to 65.2; \(P < 0.001\)), and not being a kidney transplant recipient (HR for kidney transplant recipients, 0.26; 95% CI, 0.09 to 0.73; \(P = 0.01\)). In patients with 3-month negative humoral response, a third dose (HR, 27.8; 95% CI, 5.12 to 150.0; \(P < 0.001\)) and not being a kidney transplant recipient (HR for kidney transplant recipients, 0.11; 95% CI, 0.02 to 0.74; \(P = 0.02\)) were associated with a humoral response at 6 months in a model adjusted for age, type of initial and subsequent mRNA vaccine, and baseline anti-Spike antibodies.

The limitations are a small sample size, especially for some of the CKD subgroups that did not receive a third dose; that the timing of the third dose (between the third and sixth months) was variable and not accounted for in describing these results; and that the study did not assess cellular immunity or clinical efficacy (4).

In conclusion, the pragmatic analysis of the SENCOVAC study reveals that anti-Spike antibodies continue to decrease from 3 to 6 months after vaccination in patients with CKD. A third dose of SARS-CoV-2 vaccine induces seroconversion in a high percentage of antibody-negative patients with CKD after two doses, although responses were poorer in kidney transplant recipients.

Disclosures

C. Alcaro Sánchez and E. Orero report employment with Diave-rum. D. Arroyo reports consultancy agreements with Vifor Pharma; honoraria from AstraZeneca, Boehringer Ingelheim, Eli Lilly, Gillead, GSK, Otsuka, UCB Pharma, and Vifor Pharma; and honoraria for conferences, consulting fees, and advisory boards from Amgen, AstraZeneca, Baxter, Boehringer Ingelheim, Eli Lilly, Esteve, Otsuka, Sanofi-Genzyme, and Vifor-Pharma. M.S. Pizarro Sánchez reports consultancy agreements with Alexion, Amgen, Amicus, Astellas, AstraZeneca, Bayer, Chiesi, Fresenius Medical Care, Idorsia, Kyowa Kirin, Menarini, Otsuka, Sanofi-Genzyme, and Vifor Fre-nius Medical Care Renal Pharma; research funding from Advicence, Alexion, Amgen, Amicus, Astellas, AstraZeneca, Bayer, Chiesi, Fresenius Medical Care, Idorsia, Kyowa Kirin, Menarini, Otsuka, Sanofi-Genzyme, and Vifor Fre-nius Medical Care Renal Pharma; reports consultancy agreements with Genzyme, Retrophin, and Sanofi; reports research funding from AstraZeneca, Mundipharma, and Sanofi Genzyme; reports honoraria from Advicence, Alexion, Amgen, Amicus, Astellas, AstraZeneca, Bayer, Chiesi, Fresenius Medical Care, Idorsia, Kyowa Kirin, Menarini, Otsuka, Sanofi-Genzyme, and Vifor Fre-nius Medical Care Renal Pharma; reports serving in an advisory or leadership role for the Dutch Kidney Foundation Scientific Advisory Board, European Renal Association (ERA) and Sociedad Madridileña de nefrología (SOMANE) councils, and the board of directors of Instituto de Investigación Sanitaria (IIS)-Fundacion Jimenez Diaz UAM; reports serving as a Spanish Society of Nephrology member and as Clinical Kidney Journal Editor-in-Chief; reports serving on the editorial boards of JASN, Journal of Nephrol-ogy, and Peritoneal Dialysis International; and reports speaker engagements for Advicence, Alexion, Amgen, Amicus, Astellas, AstraZeneca, Bayer, Chiesi, Fresenius Medical Care, Idorsia, Kyowa Kirin, Menarini, Otsuka, Sanofi-Genzyme, and Vifor Fre-nius Medical Care Renal Pharma. M.S. Pizarro Sánchez reports honoraria from AstraZeneca. B. Quiroga reports consultancy agreements with Amgen, Astellas, AstraZeneca, Bial, Esteve, Ferrer, Laboratorios Bial, Novartis, Otsuka, Sandoz, Sanofi-Genzyme, and Vifor-Pharma; serving in an advisory or leadership role for Amgen, Astellas, AstraZeneca, Bial, Esteve, Ferrer, Novartis, Laboratorios Bial, Otsuka, Sandoz, Sanofi-Genzyme, and Vifor-Pharma; and other interests or relationships as the secre-tary of the Spanish Society of Nephrology. J. Rojas report employment with Vircell SL. M.J. Soler reports consultancy agreements with AstraZeneca, Bayer, Boehringer, Esteve, ICU Medical, Jansen, Mundipharma, Novo Nordisk, and Travere Therapeutics; research funding from Abbvie and Boehringer; honoraria from AstraZeneca, Bayer, Boehringer, Esteve, FMC, ICU Medical, Ingelheim Lilly, Jansen, Mundipharma, Novo Nordisk, Otsuka, Traveve, and Vifor; patents or royalties for U691ES00; serving in an advisory or leadership role on the board of American Society of Nephrology news, for Ex BMC Nephrology, for CKJ, as elected Editor-in-Chief (EIC) of Clinical Kidney Journal (CKJ), as Ex ERA-EDTA council member, as Ex-Scientific Advisory Board (SAB) the European
Renal Association and the European Dialysis and Transplant Association (ERA-EDTA), for Kidney and Blood Pressure Research, and as a council member of the Spanish Society of Nephrology; speakers bureau for AstraZeneca, Bayer, Boehringer, Esteve, FMC, Jansen, Mundipharma, Novo Nordisk, and Vifor; and other interests or relationships with Sociedad Catalana de Nefrología (member) and Sociedad Española de Nefrología. S. Soriano reports honoraria for conferences and advisory boards from Astellas, Baxter, and Vifor-Pharma. S. Tejedor reports employment with Diaverum Gamapal SL. C. Toyois Ruiz reports employment with Sociedad Española de Nefrología. All remaining authors have nothing to disclose.

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Author Contributions

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The data underlying this article will be shared on reasonable request to the corresponding authors.

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Supplemental Summary 1. A list of the SENCOVAC collaborators.

References


*The list of nonauthor contributors is extensive and has been provided in Supplemental Summary 1.*

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