Clinical Kidney Journal, 2021, vol. 14, no. 12, 2612–2615

doi: 10.1093/ckj/sfab146
Advance Access Publication Date: 17 August 2021
Letter to the Editor

LETTER TO THE EDITOR

Clinical impact, reactogenicity and immunogenicity after the first CoronaVac dose in dialysis patients: a Phase IV prospective study

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CoronaVac (Sinovac Life Sciences, Beijing, China), an inactivated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine, has been approved for emergency use by 35 countries. A real-world Chilean study including 10.2 million persons showed prevention of symptomatic disease in 65.9% and severe coronvirus disease 2019 (COVID-19) in 87.5% [1]. In Brazil, CoronaVac has been included in the national vaccination program since 1 January 2021.

Among patients on chronic dialysis, the COVID-19 mortality risk was 21 times higher than that for matched historical controls [2]. Chronic kidney disease patients have been excluded from vaccine trials and had no early priority for vaccination. Therefore this single-center, Phase IV prospective 12-month follow-up study was devised to assess the clinical impact, reactogenicity and immunogenicity of CoronaVac.

Between 29 April 2021 and 8 May 2021, 198 patients ages 20–75 years were enrolled to receive a two-dose schedule of CoronaVac (3 μg each dose, 28 days apart). The study was approved by the local ethics committee and was registered at ClinicalTrials.gov (NCT04801667). All patients signed an informed consent form. On Day 28, a questionnaire was used to capture adverse reactions to the vaccine. Antibody response on Day 28 was assessed using the AdviseDx SARS-CoV-2 immunoglobulin G (IgG) II assay (Abbot Laboratories, Abbott Park, IL, USA). Values >50 AU/mL were considered positive.

The characteristics and outcomes of the study population ($n = 198$) are shown in Table 1. They were predominantly male, with a median age of 50 years [interquartile range (IQR) 40–56], diabetes mellitus in 21% and a median time on dialysis of 32 months (IQR 15–63).

The prevalence of anti-SARS-CoV-2 nucleocapsid protein on Day 0 was 27% ($n = 54$). For immunogenicity analysis, 137 patients who were seronegative for IgG anti-SARS-CoV-2 were included (56 had either positive IgG at Day 0 or a previous confirmed COVID-19 diagnosis and 5 had no serologic test available). Seroconversion 28 days after the first dose was 44% [95% confidence interval (CI) 36–53] with a median IgG value of 40 AU/mL (IQR 12–95) (Figure 1). Among those who were IgG positive, the median IgG value was 99 AU/mL (IQR 90–143). Patients >45 years of age and those on chronic-use prednisone 5 mg/day for failed renal allografts showed a lower seroconversion rate.

After the first vaccine dose, 4 (2%) patients had a COVID-19 diagnosis confirmed byreverse transcription polymerase chain reaction or antigen test at a median time of 14 days (IQR 11–15). Of these, two required hospitalization and one died 42 days after the first dose of the vaccine.

The most common adverse reaction after the first dose was local pain/tenderness (16%). Systemic symptoms (fever, myalgia, headache and diarrhea) occurred in ≤8% of the patients and no severe adverse reactions were observed.

Received: 6.8.2021; Editorial decision: 9.8.2021

Table 1. Baseline demographic characteristics, outcomes, adverse reactions and immunogenicity of the first dose of CoronaVac on dialysis patients

Parameters	Overall ($N = 198$)	Immunogenicity cohort ($n = 137$)	P-value	IgG-positive D28 ($n = 60$)	IgG-negative D28 ($n = 77$)	P-value
Demographic characteristics						
Age (years), median (IQR), *n* (%)	50 (40–56)	48 (38–56)	0.99	46 (36–56)	51 (43–57)	0.03
20–60	176 (89)	122 (89)	–	52 (87)	70 (89)	
>60	22 (11)	15 (11)	–	8 (13)	7 (9)	
Male gender, *n* (%)	106 (54)	74 (54)	0.93	32 (54)	42 (55)	0.88
Dialysis method, *n* (%)			0.23			0.40
Haemodialysis	127 (64)	79 (58)	–	37 (62)	42 (55)	
Peritoneal dialysis	71 (36)	58 (42)	–	23 (38)	35 (45)	
Time on dialysis (months), median (IQR)	32 (15–63)	29 (13–58)	0.36	29 (13–69)	28 (12–49)	0.58
Chronic kidney disease aetiology, *n* (%)						
Diabetes mellitus	41 (21)	26 (19)	0.96	10 (17)	16 (21)	0.58
Hypertension	24 (12)	17 (12)	–	9 (15)	8 (10)	–
Glomerulonephritis	41 (21)	30 (22)	–	16 (27)	14 (18)	–
Polycystic kidney disease	19 (10)	15 (11)	–	6 (10)	9 (12)	–
Unknown	54 (26)	33 (24)	–	11 (18)	22 (29)	–
Others	19 (10)	16 (12)	–	8 (13)	8(10)	–
Diabetes mellitus	51 (26)	34 (25)	0.85	14 (23)	20 (26)	0.72
Cardiovascular disease	60 (30)	37 (27)	0.51	19 (32)	18 (23)	0.28
Previous transplant	65 (33)	40 (29)	0.48	13 (22)	27 (35)	0.08
Use of prednisone	36 (18)	24 (17)	0.88	5 (8)	19 (25)	0.01
Albumin (mg/dL), mean ± SD	3.99 ± 0.4	3.98 ± 0.42	0.87	3.97 ± 0.46	3.98 ± 0.39	0.75
Outcomes ($N = 198$)		–	–	–	–	–
COVID-19 diagnosis after the first dose, *n* (%)	4 (2)	–	–	–	–	–
Age (years), median (IQR)	51 (36–63)	–	–	–	–	–
Time from first dose to COVID-19 (days), *n* (%)		–	–	–	–	–
≤7	0	–	–	–	–	–
8–14	2 (50)	–	–	–	–	–
>14	2 (50)	–	–	–	–	–
Need for hospitalization	2 (50)	–	–	–	–	–
Need for intensive care	2 (50)	–	–	–	–	–
Death	1 (25)	–	–	–	–	–
Adverse reactions to the vaccine, *n* (%)		–	–	–	–	–
Local pain or tenderness	31 (16)	–	–	–	–	–
Myalgia	15 (8)	–	–	–	–	–
Headache	11 (6)	–	–	–	–	–
Runny nose	10 (5)	–	–	–	–	–
Sore throat	6 (3)	–	–	–	–	–
Diarrhea	3 (2)	–	–	–	–	–
Fever	2 (1)	–	–	–	–	–
Serologic status before vaccination, *n* (%)		–	–	–	–	–
Negative	144 (73)	137	–	–	–	–

Table 1. (continued)

Parameters	Overall (N = 198)	Immunogenicity cohort (*n* = 137)	P-value	IgG-positive D28 (*n* = 60)	IgG-negative D28 (*n* = 77)	P-value
Positive	54 (27)	0	–	–	–	–
Indeterminate	0 (0)	0	–	–	–	–
Serologic status after the first dose, *n* (%)	–	–	–	–	–	–
Negative (<50 AU/mL)	–	77 (57)	–	–	–	–
Positive*	–	60 (44) (95% CI 36–53)	–	–	–	–
20–45 years, *n* (%)	–	29 (48) (95% CI 37–62)	–	–	–	–
>45 years, *n* (%)	–	31 (52) (95% CI 38–63)	–	–	–	–

*P = 0.04 for comparison of seroconversion rate between the two age ranges.

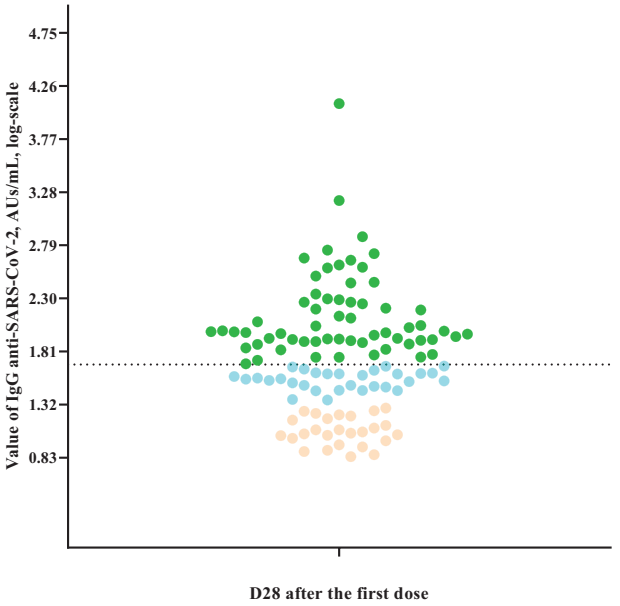

FIGURE 1: Antibody values 28 days after the first dose of the inactivated SARS-CoV-2 vaccine (*n* = 137). Abbott AdviseDx SARS-CoV-2 IgG II immunoassay for total IgG antibodies against the receptor-binding domain of the S1 subunit of the SARS-CoV-2 spike protein, in logarithmic scale. The lowest limit of detection, as per the manufacturer, is 6.8 AU/mL (0.83 log). The analytical measuring interval is 21–40 000 AU/mL. Twenty participants had undetectable values. Orange dots represent the 26 participants who had detectable values, but below the analytic limit (6.8–21 AU/mL). Light blue dots represent the 31 participants who had values above the analytic limit (>21 AU/mL or 1.32 log) but under the threshold for considering the test as positive (50 AU/mL or 1.69 log; dotted line). Green dots represent the 60 participants who tested positive for IgG antibodies.

In this ongoing prospective study, the first dose of CoronaVac vaccine was safe for dialysis patients, with a few mild adverse events. The seroconversion rate after the first dose was lower than that reported among healthcare workers receiving CoronaVac [3] but was similar to that of other studies with dialysis patients and messenger RNA (mRNA) vaccines [4]. Older age and the use of low-dose maintenance prednisone after a failed transplant were associated with a lower antibody response. These factors also impair the immunologic response to other vaccines, such as hepatitis B, in this population [5]. The small number of events and the short follow-up time prevent drawing any conclusions about the clinical effectiveness of the first dose of the vaccine.

In conclusion, our preliminary results are in agreement with previously published studies of mRNA vaccines, indicating a lower seroconversion rate among patients on renal replacement therapy. This reinforces the urgent need to maintain sanitary measures for individual protection and promote vaccination of household contacts and caregivers. Furthermore, it suggests that other immunization strategies, perhaps with higher or additional doses, or even the combination of vaccines developed using different platforms, deserve to be studied in this group of individuals.

AUTHORS' CONTRIBUTIONS

J.M.P., M.P.C., C.M.T., H.T.S. and D.T.C. participated in the research design. J.M.P., M.P.C., C.M.T., A.L.A., S.R.M. and H.T.S. wrote the article. M.P.C., C.M.T. and H.T.S. participated in the data analysis.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

ACKNOWLEDGEMENTS

This work would not have been possible without the provision of the vaccines, coordinated by Ricardo Palacios and Roberta Piorelli from Instituto Butantan, the efforts of the haemodialysis and peritoneal dialysis team led by Maria Claudia Cruz Andreoli and Camila Barbosa Silva Barros, the organization for the vaccination of patients led by Monica Rika Nakamura and Marcia Toffoli and the valuable contribution of our biochemist Elizabeth França Lucena, who conducted all the laboratory analysis.

DATA AVAILABILITY STATEMENT

Due to ethical concerns, supporting data can only be made available to bona fide researchers subject to a non-disclosure agreement.

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