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CLINICAL CASE

Immunogenicity, safety and reactogenicity of a heterogeneous booster following the CoronaVac inactivated SARS-CoV-2 vaccine in patients with SLE: a case series

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ABSTRACT

Since the COVID-19 pandemic, CoronaVac, an inactivated SARS-CoV-2 vaccine, has been widely deployed in several countries for emergency use. However, the immunogenicity of the inactivated vaccine was relatively lower when compared to other vaccine types and was even more attenuated in autoimmune patients with rheumatic disease. A third-dose SARS-CoV-2 vaccination in immunosuppressed population is recommended in order to improve immune response. However, the data were limited to those initially received mRNA or viral vector SARS-CoV-2 vaccine. Thus, we aimed to describe the safety, reactogenicity and immunogenicity of patients with systemic lupus erythematosus (SLE) who received a heterogenous booster SARS-CoV-2 vaccine following the initial CoronaVac inactivated vaccine series. Our findings support that the third booster dose of mRNA or viral vector vaccine following the inactivated vaccine is well tolerated and elicited a substantial humoral and cellular immune response in inactive patients with SLE having maintenance immunosuppressive therapy without interruption of immunosuppressive medications.

Key messages

- The immunogenicity of the CoronaVac inactivated vaccine has been shown to be lower when compared to other vaccine types and more attenuated in patients with autoimmune rheumatic disease; booster data of mRNA or viral vector SARS-CoV-2 vaccine following the inactivated vaccine in immunosuppressed patients are lacking.
- The third booster dose of mRNA or viral vector vaccine following the inactivated vaccine is well tolerated and elicits a substantial humoral and cellular immune response in inactive patients with systemic lupus erythematosus (SLE) receiving maintenance immunosuppressive therapy.
- The findings support the use of mRNA or viral vector vaccine as a third booster dose vaccine in patients with SLE who have previously received CoronaVac inactivated vaccine.

CoronaVac, an inactivated SARS-CoV-2 vaccine, has been widely deployed in several countries for emergency use. The immunogenicity of the inactivated vaccine has been shown to be substantially lower when compared with other vaccine types[1] and more attenuated in patients with autoimmune rheumatic disease.[2] Cumulative evidence suggests that a third dose of SARS-CoV-2 vaccination in immunosuppressed populations improve immune response. Booster data have so far been limited to persons initially receiving mRNA or viral vector SARS-CoV-2 vaccine.[3 4] We aimed to describe the safety, reactogenicity and immunogenicity of patients with systemic lupus erythematosus (SLE) who received a heterogeneous booster SARS-CoV-2 vaccine following an initial CoronaVac inactivated vaccine series.

Between July and August 2021, eight healthcare workers in Thailand with known SLE who had previously completed the CoronaVac series received a third booster dose of SARS-CoV-2 mRNA (Pfizer) (n=7) or adenovirus vector vaccine (ChAdOx1(1) (2)) (n=1). All were female, with a median age of 28 years (IQR 22–48 years). Half of the participants were on antimetabolite therapy or calcineurin inhibitor. Immunosuppressive medications were not altered or interrupted during the peri-booster period. The median interval between the completion of CoronaVac vaccine and the booster vaccination was 92 days (IQR 84–96) (table 1).

Table 1 Characteristics of patients with SLE receiving booster vaccine

Patient	Age	Sex	Duration of SLE* (years)	Immunosuppressive treatments	Initial vaccine series	Booster vaccine type	Days from initial to booster vaccine	Anti-RBD pan-Ig¶ by Roche Elecys (U/mL)		Anti-RBD-IgG¶ by Abbott assay (AU/mL)		sVNT‡ (% inhibition)		IFN-γ ELISpot§ (SFC/10^6 PBMCs)
								Prebooster	Postbooster†	Prebooster	Postbooster†	Prebooster (%)	Postbooster (%)†	Postbooster†
1	27	Female	5	Azathioprine 100 mg/day Ciclosporin 100 mg/day Prednisolone 10 mg/day	CoronaVac	Pfizer	113	342	24 416	275	36 182	16.74	99.70	62
2	19	Female	0	Prednisolone 10 mg/day Hydroxychloroquine 1000 mg/week	CoronaVac	Pfizer	94	83	15 076	332	25 719	27.94	98.98	228
3	50	Female	24	Mycophenolate mofetil 1000 mg/day Prednisolone 10 mg/day Hydroxychloroquine 400 mg/week	CoronaVac	Pfizer	83	50	18 213	96	26 152	<1	99.42	88
4	50	Female	13	Prednisolone 5 mg/day Hydroxychloroquine 1400 mg/week	CoronaVac	ChAdOx1	86	21	6098	170	9756	4.79	99.19	414
5	41	Female	24	Prednisolone 5 mg/day Hydroxychloroquine 1400 mg/week	CoronaVac	Pfizer	92	32	21 759	104	34 784	<1	99.48	624
6	23	Female	17	Prednisolone 5 mg/day	CoronaVac	Pfizer	72	97	15 087	300	25 955	12.56	94.95	646
7	21	Female	4	Azathioprine 100 mg/week Prednisolone 2.5 mg/day Hydroxychloroquine 1000 mg/week	CoronaVac	Pfizer	97	434	85 024	916	80 051	74.93	99.48	1200
8	29	Female	8	Tacrolimus 5 mg/day Prednisolone 2.5 mg/day Hydroxychloroquine 400 mg/week	CoronaVac	Pfizer	92	NA	71 508	NA	96 572	NA	99.64	NA

*Systemic lupus erythematosus.
†14 days after booster vaccination.
‡SARS-CoV-2 Surrogate Virus Neutralization Test (NeutraLISA, Euroimmun, Lübeck, Germany) reported as % neutralisation.
§IFN-γ ELISpot reported as spot-forming cell per million peripheral blood mononuclear cells.
¶Anti-SARS-CoV-2 spike receptor binding domain (RBD) IgG antibody concentrations reported as .U/mL or AU/mL.
ELISpot, enzyme-linked immunosorbent spot ; IFN-γ, interferon gamma; NA, not applicable; SFC, spot-forming cell; SLE, systemic lupus erythematosus.

Prior to the booster dose, all patients had low-positive antispike antibodies with a median level of 83.3 (IQR 31.6–341.6) U/mL, which rose to a median of 19,986 (IQR 15 079–59 735) U/mL at day 14 after the booster vaccination (table 1). Antinucleocapsid antibodies were undetectable in patients 7 and 8, who had a robust humoral response, implying that there was no recent COVID-19 infection resulting in the high antibody titre. NeutraLISA (Euroimmun, Lübeck, Germany) was used to test prebooster and postbooster samples for neutralising activity against the SARS-CoV-2 wild type. Before the booster vaccination, all except patient 7 had negative sVNT results (<35% inhibition). After the booster dose, all patients elicited a strong immune response with at least 95% inhibition.

Cellular immunogenicity was assessed at day 14 after the booster vaccination using direct ex vivo interferon gamma enzyme-linked immunosorbent spot assay with peripheral blood mononuclear cells. The majority of patients had strong cellular immune responses, except patients one and three who received more intensive immunosuppressive therapy including mycophenolate mofetil, azathioprine and calcineurin inhibitor (62–88 spot-forming cells/10^6 per million peripheral blood mononuclear cells (PBMC)). While patient 4, who received a viral vector booster, had a lower humoral response (antispike antibody 6098 U/mL vs 15 076–85 024 U/mL in mRNA booster), the cellular immunogenicity was comparable to those receiving the mRNA booster.

During the study period, none of the patients experienced an SLE flare. The reactogenicity was mild and self-limiting but more prevalent in the booster dose than in the initial CoronaVac vaccination (online supplemental figure 1). The most common complaint was injection site pain followed by fatigue and fever.

Given the growing concern regarding the immunogenicity of the inactivated vaccine in immunosuppressed autoimmune patients, this is the first study to show improved humoral and cellular response to the heterogeneous booster vaccine in patients with SLE who had previously received an inactivated vaccine. In our SLE cohort, we observed a stronger humoral immunogenicity to an additional vaccine dose than previously reported among organ transplant recipients, autoimmune disease patients and healthy individuals receiving triple-dose CoronaVac vaccines.[3–5] This is possibly due to the younger age, lower immunosuppressive therapy, and different initial and booster vaccine types in our cohort. It is known that the cellular immune response caused by inactivated vaccines is generally weak. Our findings show that a booster dose of mRNA or viral vector vaccine enhanced strong cellular immune responses, though responses were weaker in those given an antimetabolite or calcineurin inhibitor.

This study is limited by its observational study design and small sample of patients. It also may not offer generalisability to active patients with SLE having a higher dose of immunosuppressive therapy.

The SARS-CoV-2 pandemic continues to put immunosuppressed autoimmune patients at great risk of severe disease and death. Data attempting to isolate an optimum SARS-CoV-2 vaccine regimen for this group are scarce. Our findings provide support that the third booster dose of mRNA or viral vector vaccine following the inactivated vaccine is well tolerated and elicit a substantial humoral and cellular immune response in inactive patients with SLE receiving maintenance immunosuppressive therapy. Further studies are required to tailor the vaccine regimen according to a person's immune status.

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