IMMUNOSUPPRESSIVE THERAPY: IMPACT ON ANTIBODY RESPONSE TO AN INACTIVATED SARS-COV-2 VACCINE IN SYSTEMIC LUPUS ERYTHEMATOSUS

Emily Figueiredo Neves Yuki^{1,*}, Eduardo Ferreira Borba¹, Sandra Gofinet Pasoto¹, Luciana Parente Seguro¹, Michelle Lopes¹, Carla Gonçalves Schahin Saad¹, Ana Cristina Medeiros-Ribeiro¹, Clovis Artur Silva¹, Danieli Castro Oliveira de Andrade¹, Léonard de Vinci Kanda Kupa¹, Camilla Hoff¹, Isabela Bertoglio¹, Juliana Valim¹, Francisco Fellipe Claudino Formiga¹, Lorena Betancourt¹, Tatiana Pedrosa Nascimento¹, Nadia Emi Aikawa¹, Eloisa Silva Dutra de Oliveira Bonfá¹

1.Universidade de São Paulo, São Paulo (SP), Brazil.

*Corresponding author: emilymed93@gmail.com

BACKGROUND

SARS-CoV-2 immunogenicity in systemic lupus erythematosus (SLE) has been described mostly in small number of patients and with mRNA vaccines. The only two large studies, one with Sinovac-CoronaVac (SARS-CoV-2 inactivated vaccine) and the other with mRNA vaccine have performed an overall analysis of several autoimmune rheumatic diseases, but the accurate impact of SLE and/or its therapy remains to be determined. The objective of this work was to assess factors associated with antibody response to an inactivated SARS-CoV-2 vaccine (Sinovac-CoronaVac) and the safety of this immunogen in SLE patients.

METHODS

We conducted a prospective controlled study of 232 patients with SLE and 58 healthy controls (CTRL) (4SLE:1CTRL), who were vaccinated with two doses of CoronaVac with a 28-days interval. Immunogenicity analysis included anti-SARS-CoV-2 S1/S2 IgG seroconversion (SC), anti-S1/S2 IgG geometric mean titers (GMT), neutralizing antibodies (NAb) positivity and median neutralizing activity. Immunogenicity's primary outcome was assessed by anti-SARS-CoV-2 IgG and NAb 6 weeks after the second dose (D69) in patients without prior COVID-19. The influence of immunosuppressors on immune response at D69 was also assessed. Safety was assessed through D0-D69.

RESULTS

Patients and CTRL were well balanced for age ($p = 0.771$) and sex ($p > 0.999$). At D69, SLE patients showed a moderate but significant lower anti-SARS-CoV-2 IgG SC (70.2% vs. 98.1%, $p < 0.001$) and GMT (29.6 [95%CI = 24.8–35.4] vs. 77.0 [95%CI = 64.5–91.8], $p < 0.001$) and frequency of NAb positivity (61.5% vs. 84.6%, $p = 0.002$) compared to CTRL, but with similar neutralizing activity (56.2% vs. 65.9%, $p = 0.132$) between groups. Factors associated with lower immunogenicity (IgG SC and NAb positivity) at D69 were prednisone use ($p < 0.001$), immunosuppressive use ($p < 0.001$), especially mycophenolate mofetil (MMF) ($p < 0.001$). Hydroxychloroquine use was associated in the univariate analysis with higher SC ($p = 0.009$). Systemic lupus erythematosus patients under hydroxychloroquine monotherapy showed similar SC to CTRL at D28 (46% vs. 45.2%, $p = 0.942$) and D69 (100% vs. 98.1%, $p = 1.000$). In the multivariate analysis, prednisone and also MMF use were independently associated with both lower SC ($p < 0.001$) and NAb positivity ($p < 0.001$). Safety analysis revealed no moderate/severe adverse events.

CONCLUSION

Sinovac-CoronaVac has an excellent safety profile and moderate immunogenicity in SLE patients, although lower than CTRL. Prednisone and MMF have a deleterious effect in this immune response reinforcing the need to investigate the role of temporary MMF withdrawn to improve immunogenicity. (clinicaltrials.gov #NCT04754698 [CoronavRheum]).

FUNDING

Funded by FAPESP, CNPq and B3 – Bolsa de Valores do Brasil.

KEYWORDS

Anti-SARS-CoV-2 IgG, Systemic lupus erythematosus, SARS-CoV-2 vaccine, Immunogenicity, Neutralizing antibodies.