PROSPECTIVE CONTROLLED TRIAL OF IMMUNOGENICITY AND SAFETY OF AN INACTIVATED VIRUS VACCINE AGAINST SARS-COV-2 IN PATIENTS WITH SYSTEMIC SCLEROSIS.

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BACKGROUND

Considering that the lung is frequently affected in systemic sclerosis (SSc) and also the main target organ in SARS-CoV-2 infection, it is of great interest to define the immunogenicity of the COVID-19 vaccine in these patients, as well as the possible impact of immunosuppressant drugs.

METHODS

This is a phase 4 prospective study that analyzed immunogenicity/safety of two doses of inactivated SARS-CoV-2 vaccine (CoronaVac) in 51 patients classified as SSc according to the ACR/EULAR criteria and compared to a control group of 153 healthy individuals. Anti-SARS-CoV-2 S1/S2 IgG and neutralizing antibodies (NAb) were assessed at each vaccine shot and 6 weeks after the 2nd dose, while vaccine adverse events (AEs) were recorded at each visit. Statistical significance was set at $p < 0.05$.

RESULTS

Patients and controls had comparable median (interquartile range – IQR) ages (47.5 [38.3–57] vs. 48 [38–57], $p = 0.945$) and female (both 94.1%; $p > 0.999$) predominance. Patients had predominantly the diffuse SSc (68.6%) subtype, and the most frequent clinical manifestations were esophageal dysmotility (80.4%), interstitial lung disease (74.5%) and pitting scars (70.6%), with predominance of positive anti-Scl-70 antibody (60.8%). Immunosuppressants were currently used by 70.6% of patients, mainly mycophenolate mofetil (51%). Seroconversion rates (SC) were similar in SSc patients and controls after the first dose (35.9% vs. 36.4%, $p = 0.958$), with a significant increase after the second dose, particularly in the control group (64.1% vs. 94.2%, $p < 0.001$). Anti-SARS-CoV-2 S1/S2 IgG titers were similar in SSc patients and controls after the first dose (7.3 [4.9–11.0] vs. 10.9 [8.7–13.7], $p = 0.370$), with a significant increase after the second dose, especially in the control group (26.4 [16–43.6] vs. 66.9 [58.6–76.4]; $p < 0.001$). Neutralizing antibodies positivity was comparable in both groups after the first dose (38.5% vs. 33.1%, $p = 0.537$) whereas after the second dose, the positivity was higher in the control group (53.8% vs. 76.9%; $p = 0.006$). Multiple regression analysis pointed current use of mycophenolate as associated with insufficient seroconversion (odds ratio [OR] = 0.056 [95% CI = 0.009–0.034], $p = 0.002$) and positivity for NAb (OR = 0.047 [95% CI = 0.007–0.036], $p = 0.002$), whereas no effect was observed for disease subtype ($p > 0.05$). Inactivated SARS-CoV-2 vaccine was overall well tolerated by all participants, with only mild AEs in both groups, especially pain at injection site, malaise, headache, somnolence, diarrhea and sore throat.

CONCLUSION

CoronaVac has shown an excellent safety profile and reasonable rates of immunogenicity in patients with SSc, not influenced by disease subtype. Mycophenolate mofetil was the only factor associated with a substantial deleterious effect on immunogenicity. This specific group will probably require specific strategies, including social distancing and other measures to be defined in future studies, such as temporary discontinuation of mycophenolate mofetil and booster dose.

KEYWORDS

Systemic sclerosis, COVID-19, Vaccine, Immunogenicity, Safety.