SARS-COV-2 VACCINE IN PATIENTS WITH RHEUMATOID ARTHRITIS: ATTENUATED RESPONSE INDUCED BY SPECIFIC DMARD, DMARD COMBINATION AND PREDNISONE

Ana Cristina de Medeiros Ribeiro^{1,*}, Karina Bonfiglioli¹, Diogo Domiciano¹, Andrea Shimabuco¹, Henrique Carriço¹, Carla Saad¹, Emily Yuki¹, Sandra Gofinet Pasoto¹, Tatiana Pedrosa¹, Carlo Renner Araújo¹, Matheus Rodrigues Silva¹, Tatiane Lie Nakai¹, Guilherme Balbi¹, Clóvis Silva¹, Nádia Aikawa¹, Eloisa Silva Dutra de Oliveira Bonfá¹

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

*Corresponding author: anademedeiros@yahoo.com

BACKGROUND

Due to the COVID-19 pandemic, there is a pressing need to evaluate the immune response to SARS-CoV-2 vaccines in rheumatoid arthritis (RA) patients, and identify the factors that can affect the immunogenicity in such population.

METHODS

This is a phase 4 prospective study that analyzed immunogenicity/safety of two doses of inactivated SARS-CoV-2 vaccine (CoronaVac) in 260 seronegative RA patients in comparison to a group of 104 controls (CG), in a 5:2 ratio. Seroconversion (SC) of anti-SARS-CoV-2 S1/S2 IgG and the positivity of neutralizing antibodies (NAb) were assessed 28 days after the first dose (D28) and 6 weeks after the second dose (D69), while vaccine adverse events (AEs) were recorded at each visit. Disease activity status measured by clinical disease activity index (CDAI) and C reactive protein (CRP)-based disease activity score with 28 joints (DAS28-CRP), and use of disease modifying antirheumatic drugs (DMARD) were assessed at recruitment using the last electronic record. Statistical significance was set at $p < 0.05$.

RESULTS

The groups had comparable median (interquartile range – IQR) ages (59 [50–65] vs. 58 [49.8–64], $p = 0.483$) and female (both 90.4%; $p > 0.999$) predominance. Median (IQR) disease duration was 19 (11–26) years. Most of patients had rheumatoid factor positivity (77.8%) and anti-CCP positivity (69.7%). The median (IQR) baseline CDAI was 8.5 (4–16) and DAS28-CRP was 2.9 (2.2–4). Rheumatoid arthritis patients had lower SC at D28 (10.8% vs. 30.1%; $p < 0.001$) and D69 (61.8% vs. 94.2%; $p < 0.001$) in comparison to CG. Similarly, RA patients also had lower positivity for NAb at D28 (13.9% vs. 32%; $p < 0.001$) and D69 (45% vs. 78.6%; $p < 0.001$). Univariate analysis pointed older age ($p < 0.001$), methotrexate ($p = 0.003$), abatacept ($p < 0.001$) and the combination of ≥ 2 DMARDs ($p = 0.019$) as associated with absence of SC, while older age ($p < 0.001$), prednisone ($p = 0.045$) and abatacept ($p = 0.038$) were associated with absence of NAb. In contrast, sulfasalazine ($p = 0.035$) was positively associated with SC. Baseline disease activity did not interfere with immunogenicity parameters ($p > 0.05$). After multivariate analyses, factors independently related to SC were: older age (odds ratio, OR = 0.79 [0.70–0.89] for each 5-year interval; $p < 0.001$), methotrexate use (OR = 0.50 [0.28–0.91]; $p = 0.024$), abatacept use (OR = 0.36 [0.18–0.70]; $p = 0.003$), combination of ≥ 2 DMARDs (OR = 0.50 [0.26–0.97]; $p = 0.041$), and sulfasalazine use (OR 3 [1.04–8.75]; $p = 0.043$). Regarding the presence of NAb, age over 60 years (OR = 0.54 [0.33–0.90]; $p < 0.018$) and prednisone use (OR = 0.57 [0.33–0.99]; $p < 0.046$) were negatively related to presence of NAb. No moderate/severe adverse event occurred.

CONCLUSION

We have observed that RA patients have a low/moderate reduced immunogenicity to SARS-CoV-2 vaccine. The novel evidence that specific DMARD, DMARD combination and prednisone are the most relevant factors to impair vaccine antibody response in this disease reinforces the need of a distinct approach to improve vaccine response in this population.

KEYWORDS

SARS-CoV-2 vaccine, Rheumatoid arthritis, Immunogenicity.