RHEUMATOLOGY

Letter to the Editor (Other)

Antibody responses to inactivated and mRNA SARS-CoV-2 vaccines in familial Mediterranean fever patients treated with interleukin-1 inhibitors

Rheumatology key message

- Both BNT162b2 and CoronaVac were immunogenic in FMF patients who were on IL-1 inhibitors and treatment cessation before vaccination was not needed.

DEAR EDITOR, During the coronavirus disease 2019 (COVID-19) pandemic, the disease course of COVID-19 and vaccine responses in patients with autoinflammatory diseases have been among the topics of interest in rheumatology. Familial Mediterranean fever (FMF) is the most common monogenic autoinflammatory disease and some studies have been published regarding the relationship between FMF and COVID-19. The incidence or severity of COVID-19 in FMF patients was not found to be different from that of the non-FMF population [1]. There are data regarding the safety of COVID-19 vaccines in patients with autoinflammatory disorders taking biologics [2], yet there are not enough data regarding the antibody responses to the vaccines. We therefore measured the antibody responses of FMF patients on IL-1 inhibitors who were vaccinated with CoronaVac (Sinovac Biotech, Beijing, China) or BNT162b2 (Pfizer-BioNTech).

Study participants consisted of FMF patients who were followed up in our rheumatology clinic. They were either on anakinra or canakinumab and did not receive any other immunosuppressive treatment. A total of 48 patients agreed to participate: 35 patients were vaccinated with CoronaVac and 13 patients were vaccinated with BNT162b2. Due to logistical issues, there was only one control group, consisting of 96 age- and sex-matched volunteers who were vaccinated with CoronaVac. Details of the study participants can be found in Supplementary Table S1, available at *Rheumatology* online. Vaccines were administered to the patients twice with a 1 month interval. The first doses were administered between 14 January and 14 July 2021 and the second doses were administered between 13 February and 31 August 2021. Blood samples were collected 14 days after each dose.

This study was approved by the Ethics Committee of Cerrahpasa Medical Faculty, Istanbul University-Cerrahpasa. Informed consents were obtained from each participant. The study was conducted in accordance with the Helsinki Declaration.

The SARS-CoV-2 IgG II Quant assay, which is a chemiluminescent microparticle immunoassay manufactured by Abbott Laboratories (Abbott Park, IL, USA), was used to detect IgG antibodies against the spike receptor-binding domain (RBD) of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The AdviseDx SARS-CoV- 2 IgG II test results are in [arbitrary units (AU)/ml]. The cut-off value is 50.0 AU/ml, thus values <50.00 AU/ml were accepted as negative and values ≥50.0 AU/ml were accepted as positive.

FMF patients vaccinated with BNT162b2 and CoronaVac had median antibody levels of 14 593 AU/ml and 574 AU/ml, respectively. The control group had a median antibody level of 745 AU/ml ($P < 0.001$). However, FMF patients and the control group who were vaccinated with CoronaVac had no significant difference in their antibody levels after either dose ($P = 0.147$). The 13 (100%) FMF patients vaccinated with BNT162b2 had positive antibody titres after the second dose, whereas 33 (94.3%) FMF patients vaccinated with CoronaVac and 95 (99%) controls had positive antibody titres after the second dose ($P = 0.218$).

FMF patients vaccinated with BNT162b2 had higher antibody titres compared with the FMF patients vaccinated with CoronaVac after the second dose (18 785 ± 14 782 *vs* 3161 ± 6537 AU/ml; $P < 0.001$) (Fig. 1). However, the antibody titres after the first dose did not differ significantly between the groups (15 184 ± 19 427 *vs* 753 ± 3077 AU/ml; $P = 0.075$). FMF patients who previously had COVID-19 had higher antibody titres after the second dose than FMF patients who did not contract COVID-19 (15 156 ± 15 317 *vs* 5349 ± 9748 AU/ml; $P = 0.016$).

This study showed no significant difference in the antibody responses to CoronaVac between the FMF patients who are on IL-1 inhibitors and the control group. Previously a study found that adult patients on canakinumab who received influenza and meningococcal vaccines had post-vaccination antibody titres comparable to those of the controls [3]. The use of anakinra was not found to affect the antibody response to SARS-CoV-2 infection [4], although a correspondence reported that the use of IL-1 inhibitors affected the neutralizing activity of anti-SARS-CoV-2 antibodies [5]. Our study is in line with the majority of the literature by showing no appreciable effect of IL-1 use on antibody levels.

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Fig. 1 SARS-CoV-2 IgG antibody titres of the FMF and control patients after the second dose of vaccinations
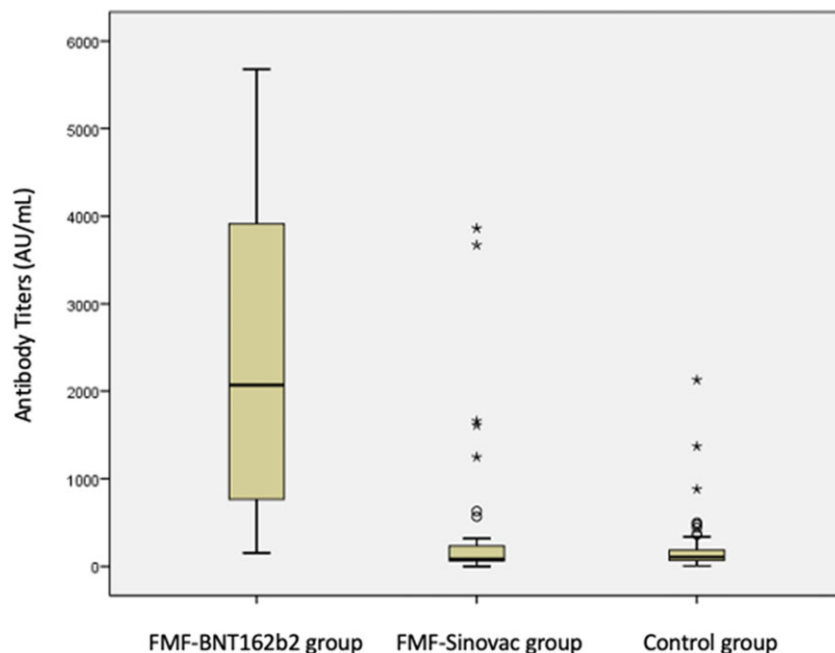
The patients had higher antibody levels when vaccinated with BNT162b2 compared to CoronaVac. A study that compared BNT162b2 and CoronaVac vaccines in a normal population also reported higher antibody levels after two doses of BNT162b2 compared to CoronaVac [6]. Thus, lower antibody titres in response to inactivated vaccines are also seen in the general population.

There were several limitations in this study. Vaccine hesitancy made it hard to find participants for the study and resulted in a moderate sample size. Turkey's late rollout of BNT162b2 resulted in more patients getting vaccinated with CoronaVac when this study was planned. A control group for BNT162b2 could not be included due to logistical issues. Some patients gave blood samples only after the first dose and we had to rely on the patients' self-reports for previous COVID-19 infections. Larger studies with different COVID-19 vaccines are needed to support vaccine recommendations.

Our study reiterates the recommendations of the guidelines [7, 8] that urge patients who are on IL-1 inhibitors to get vaccinated without altering their treatment. Inactivated and mRNA SARS-CoV-2 vaccines were immunogenic in FMF patients using IL-1 inhibitors, although the mRNA vaccine produced higher antibody titres. Nevertheless, the most important thing is to make sure the patients on IL-1 inhibitors get vaccinated with whichever vaccine is available.

Data availability statement

The data underlying this article will be shared upon reasonable request to the corresponding author.

Supplementary data

Supplementary data are available at *Rheumatology* online.

Serdal Ugurlu [iD][1], **Ruveyda Akcin**[2], **Ali Yagiz Ayla** [iD][1], **Bekir Kocazeybek**[2], **Mert Oztas** [iD][1], **Gunay Can**[3], **Leyla Mustafayeva**[4], **Nese Saltoglu**[5], **Betul Yilmaz**[1] and **Huri Ozdogan**[1]

[1]*Division of Rheumatology, Department of Internal Medicine,* [2]*Department of Medical Microbiology,* [3]*Department of Public Health,* [4]*Department of Physical Medicine and Rehabilitation and* [5]*Department of Infectious Diseases, Cerrahpasa Medical Faculty, Istanbul University-Cerrahpasa, Istanbul, Turkey*
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Correspondence to: Serdal Ugurlu, Division of Rheumatology, Department of Internal Medicine, Cerrahpaşa Medical Faculty, Istanbul University-Cerrahpaşa, Fatih, Istanbul 34098, Turkey. E-mail: serdalugurlu@gmail.com

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