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The Anti-SARS-CoV-2 IgG Antibody Response of Participants Vaccinated with Different Vaccine Combination

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Abstract

Introduction: In current literature, there are lots of description about the new Coronavirus, named as SARS-CoV-2 by World Health Organization (WHO). Basically, SARS-CoV-2 has been described as the agent of COVID-19 disease which was reported a group of patients with pneumonia of unknown cause in Wuhan, China, in December 2019. In this work, our aim was to investigate the anti-S1 IgG response that occurs after different kinds and different doses of SARS-CoV-2 vaccines and the demographic characteristics of participants.

Materials and Methods: A total of 299 participants were included in this study to detect the Anti-SARS-CoV-2 IgG antibody. The only inclusion criteria for this study were being vaccinated minimum two-doses of any SARS-CoV-2 vaccine. For detecting the antibody levels of participants, Anti-SARS-CoV-2 ELISA (IgG) test kit which applies a recombinant S1 subunit of the SARS-CoV-2 spike protein, enabling detection of IgG antibodies was used.

Results: Out of 299 individuals, 128 (42.8%) were male and 171 (57.2%) were female in our study. The mean age of individuals 35.11±8.13 (minimum: 19 and maximum: 59). The lowest antibody levels were belonging to Group 2 and Group 3 (138.66±25.41, and 82.09±63.42 IU/ml, respectively), while the highest antibody levels were belonging to Group 6 (239.35±18.73 IU/ml).

Discussion: According to our results, a significantly higher humoral immunogenicity of the SARS-CoV-2 BioNTech compared with the CoronaVac vaccine. A significant increase in serological response was achieved with the 3rd or 4th dose of vaccine; however, it had better to be vaccinated with BioNTech after 2nd dose of COVID-19 vaccine.

Keywords: SARS-CoV-2, COVID-19, Antibody response, CoronaVac, BioNTech

Introduction

In current literature, there are lots of description about the new Coronavirus, named as SARS-CoV-2 by World Health Organization (WHO). Basically, SARS-CoV-2 has been described as the agent of COVID-19 disease which was reported a group of patients with pneumonia of unknown cause in Wuhan, China, in December 2019 (1-3). According to WHO data, there are 760.897.555 confirmed cases, and 6.874.585 confirmed death of COVID-19 till the beginning of pandemic (December 2019) (4).

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According to the genome organization of SARS-CoV-2 virus, the vaccines trigger a powerful immune response against the spike (S) protein of virus which antibodies can bind the receptor-binding domain (RBD) and neutralizing epitopes (5, 6). There are different types of vaccines, including mRNA, vector, and inactivated vaccines, and, two different SARS-CoV-2 vaccines (mRNA and inactivated) were mostly preferred and used in pandemic. Firstly, the mRNA-based vaccine of BioNTech (Pfizer, Germany) candidate that contains modified mRNA to encode only the RBD portion of the S protein, thought to be the key target of virus-neutralizing antibodies (6, 7). Secondly, the inactivated vaccine of Sinovac (CoronaVac, Sinovac Life Sciences Co., Ltd. Beijing, China) has a strong immunogenic effects especially in healthy adult participants who were above 60 years-old (8). In the first two years of SARS-CoV-2 pandemic, lots of people all around the world has been vaccinated two or more doses of those vaccines.

In this work, our aim was to investigate the anti-S1 IgG response that occurs after different kinds and different doses of SARS-CoV-2 vaccines and the demographic characteristics of participants.

Materials and Methods

Ethical Statement: The Local Ethics Committee of Kafkas University Faculty of Medicine (Approval date: 22.09.2021; Approval number: 80576354-050-99-192) was evaluated and approved the current study. The authors were careful for all procedures of this work and obey all the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Participants and Experimental Groups: In this work, a total of 299 participants were included to detect the Anti-SARS-CoV-2 IgG antibody. The only inclusion criteria for this study were being vaccinated minimum two-doses of any SARS-CoV-2 vaccine, CoronaVac (CoronaVac, China) and BioNTech (BioNTech, Fosun Pharma, Pfizer, Germany). Different kinds of vaccine combinations were available in our study and the experimental groups were consisted as seen in Table 1.

Table 1: Experimental groups of our study

Group name	Participants (n)	Vaccine combination
Group 1	50	two-doses of CoronaVac
Group 2	42	two -doses of BioNTech
Group 3	50	three-doses of CoronaVac
Group 4	58	three-doses of BioNTech
Group 5	50	two-doses of CoronaVac and one-dose of BioNTech
Group 6	49	two-doses of CoronaVac and two-doses of BioNTech

The blood samples were taken after 4 weeks from the final dose of vaccine. Each participant was informed about the study and 8-10 ml blood samples were taken into blood tubes. After a centrifugation at 3500 rpm for 10 minutes, the serum samples were separated and stored at -80 ^{o}C till the experiment day. Additionally, the demographic data were obtained from each participant.

Anti-SARS-CoV-2 IgG Antibody Detection by ELISA: Anti-SARS-CoV-2 IgG ELISA test kit (Cat no: EI-2606-9601-10-G, Euroimmun, Germany) which applies a recombinant S1 subunit of the SARS-CoV-2 spike protein was used for detecting the antibody levels of patients. All chemicals, solutions and supplies including 96-well microplates were firstly brought to room temperature. The first and second wells were used for the negative and positive controls, respectively. Then, serially diluted standards (1 RU/ml, 10 RU/ml, 20 RU/ml, 40 RU/ml, 80 RU/ml, and 120 RU/ml, respectively) were pipetted into the 3-8 wells, respectively. 1/101 diluted samples (100 µl) were added to each well between 9-96. After incubation for 60 min at 37°C, for 60 min, washing with washing solution (5 times), and adding 100 µl enzyme conjugate were performed to each well. After the same washing protocol (5 times with washing solution), 100 µl of chromogen/substrate solution was added and

incubated at 37 °C for 30 min under darkened conditions. As a last step of ELISA study, 100 µl stop solution was added to all microplate wells and the plate was read at a wavelength of 450 nm by Multiskan™ GO UV/Vis microplate spectrophotometer (Thermo Scientific, Schwerte, Germany).

Results were evaluated by calculating a ratio of the OD of the samples over the OD of the calibrators ranging from 1-120 RU/ml. Quantitative results obtained in RU/ml were converted to International Units (IU/ml) by multiplying 3.2 in accordance with WHO specifications. If the ratio was under 25.6 IU/ml, it was considered as negative; if it was between 25.6 and 35.2 IU/ml, it was considered as borderline positive; and if it was above 35.2 IU/ml, it was considered as positive.

Statistical Analysis: The data were analyzed using the IBM SPSS version 21.0 statistical software (IBM, Armonk, NY, USA). The "number (n)," "percentage (%)," "mean," "standard deviation (SD)," minimum and maximum values were given for the descriptive statistics. The independent samples t-test or Mann-Whitney U test were used to compare numerical variables. All the p-values were based on a two-sided test of statistical significance and significance was accepted at the level of $p < 0.05$.

Result

Out of 299 individuals, 128 (42.8%) were male and 171 (57.2%) were female in our study. The mean age of individuals 35.11±8.13 (minimum: 19 and maximum: 59). The age and gender information is seen in Table 2. The experimental groups had different serum antibody levels. As seen in Table 2, the lowest antibody levels were belonging to Group 2 and Group 3 (138.66±25.41, and 82.09±63.42 IU/ml, respectively), while the highest antibody levels were belonging to Group 6 (239.35±18.73 IU/ml). When the groups were checked, it was seen that the lowest mean antibody levels were belongs to the participants who had been vaccinated only CoronaVac; and the highest mean antibody levels were belongs to the participants who had been vaccinated with a vaccine combination that contained BioNTech.

Table 2: All data about the participants

	Gender (n %)		Age		The level of Anti-SARS-CoV-2 IgG	
	Male	Female	Range	Mean±SD	Range	Mean±SD
Group 1	22 (44%)	28 (56%)	19-48	31.38±6.21	14.72-218.57	138.66±25.41
Group 2	22 (52.4%)	20 (47.6%)	20-57	30.52±10.62	153.60-269.70	224.21±31.11
Group 3	18 (36%)	32 (64%)	29-53	37.80±5.84	15.60-225.70	82.09±63.42
Group 4	20 (34.5%)	38 (65.5%)	20-59	38.31±8.29	91.50-268.30	232.84±40.64
Group 5	20 (40%)	30 (60%)	23-47	33.22±6.87	205.50-259.70	234.46±16.60
Group 6	26 (53%)	23 (47%)	24-47	34.41±5.99	194.10-274.40	239.35±18.73

The statistical analysis showed that there was significant difference between experimental groups ($p<0.001$). There were significant difference between Group 1 and all other experimental groups ($p<0.001$); however, there were no statistically significant difference between Group 2, Group 4, Group 5, and Group 6 (Figure 1).

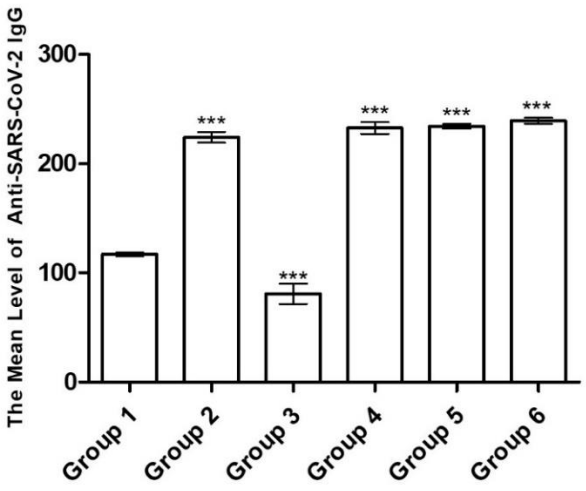

Figure 1: The mean level of Anti-SARS-CoV-2 IgG antibody in all experimental groups

Discussion

The various COVID-19 vaccines were shown relay great efficiency to reduce the severity, morbidity, and mortality of COVID-19 disease (9). Different kinds of SARS-CoV-2 vaccines (inactivated and mRNA-based) have different efficiency according to the applied vaccine doses. According to the WHO data, there are 13.232.780.775 dose vaccine have been applied all over the world (4).

On the other hand, quantitative determination and follow-up the anti-SARS-CoV-2 antibodies after vaccination is quite important to detect and show the humoral immune response (10). In this study, we aimed to show the mean levels of Anti-SARS-CoV-2 IgG antibody in participants who had been vaccinated by 2-, 3-, and 4-doses of SARS-CoV-2 vaccine. The results showed that being vaccinated may protects the people from the severity and mortality of COVID-19 disease; however, it has been proven that preferring the most effective vaccine combination is more important. According to our results, being vaccinated by a vaccine combination including BioNTech is more effective than being vaccinated by a vaccine combination including only CoronaVac. Two-doses of BioNTech, three-doses of BioNTech, two-doses of CoronaVac and one-dose of BioNTech, and two-doses of CoronaVac and two-doses of BioNTech caused more effective humoral response in participants.

According to the literature, the antibody response occurred by the inactivated vaccine (CoronaVac) started to decrease in 3rd-5th months after vaccination (11, 12). SARS-CoV-2 antibody response was evaluated in various studies before the 3rd dose vaccination in our country. In these studies the participants had been vaccinated by a 3rd dose of vaccine (CoronaVac or BioNTech), and the mean levels of IgG antibody were evaluated. It was determined that 3rd dose vaccination led to a dramatic increase in the mean levels of IgG antibody in participant (12-14). Our results are parallel with the current data; however, the increase was especially detected in participant who had vaccinated at least one BioNTech vaccine.

A general view in literature is that vaccination with BioNTech induces stronger humoral responses than CoronaVac (15). A study reported that a higher humoral immune response was observed with BioNTech compared with CoronaVac after two doses and after the BioNTech booster vaccination (16). Another study also stated that IgG seropositivity was lower after CoronaVac than after BioNTech and declined over time since vaccination for CoronaVac recipients but not BioNTech recipients (17). Additionally, a two-dose vaccination scheme with CoronaVac induces lower levels of anti-SARS-CoV-2 spike antibodies than BioNTech in a broad age range. Furthermore, antibody production declines with time in individuals vaccinated with CoronaVac and less noticeably, with BioNTech (11, 18, 19).

According to our results, a significantly higher humoral immunogenicity of the SARS-CoV-2 BioNTech compared with the CoronaVac vaccine. The limitations of the study are that the neutralizing antibody response and cellular immunity could not be evaluated and the sample size was small. As a conclusion, a significant increase in serological response was achieved with the 3rd or 4th dose of vaccine; however, it had better to be

vaccinated with BioNTech after 2nd dose of COVID-19 vaccine.

Declaration of Interest: The author declares that there is no conflict of interest regarding the publication of this paper.

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