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Side effects of the BNT162b2 vaccine in the personnel of the Military Central Hospital

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Abstract. – OBJECTIVE: The pandemic disease by SARS-CoV-2 infection does not have an effective treatment. To prevent the disease, scientists developed vaccines that the clinicians use as an emergency licensed vaccine. The objective of this study was to determine the side effects in personnel vaccinated at the Military Central Hospital of Mexico with the BNT162b2 vaccine.

PATIENTS AND METHODS: This study included the subjects who had received both doses of the BNT162b2 vaccine between December 2020 and February 2021. We asked about the side effects after the first and the second vaccine doses. One group had no history of COVID-19, and the second had a history of COVID-19. ANTI-SARS-CoV-2 antibodies were measured by the immunodetection technique in the second group only.

RESULTS: We included 946 participants, 62% were women, and 80% were without comorbidities; 680 were included in the first group, and only 266 were in the second group. After the first dose, 77% of the first group and 86% of the second group presented some side effects. After the second dose, 84% of the first group and 89% of the second group showed some side effects. The main side effect was mild pain. All participants (126) were IgG positive, and only 26.9% were IgM positive at 17.5 days (12.8 days, 20.3 days) after the second dose.

CONCLUSIONS: There is a positive correlation between side effects after the first dose in patients with a history of previous SARS-CoV-2 infection compared to those who did not. Nevertheless, this correlation is not present after the second dose. The low percentage of IgM could be related to the time interval between vaccination and sample measure.

Key Words:
COVID-19 vaccine, Side effects, Antibody, Mexico.

Introduction

In December 2019, an outbreak of atypical pneumonia of unknown viral origin emerged in Wuhan, China. In January 2020, the beta-coronavirus SARS-CoV-2 (severe acute respiratory syndrome coronavirus) was identified as the etiological agent, which causes the infectious disease known worldwide as COVID-19 (coronavirus disease 2019). It was declared a pandemic on March 11, 2020, by the World Health Organization (WHO)[1].

The most common symptoms are fever, cough, chest pain, myalgia, and fatigue. Other symptoms include sputum production, headache, hemoptysis, diarrhea, dyspnea, and lymphopenia. In addition, chest computed tomography findings are bilateral ground-glass opacity lesions[2,3].

About 80% of the patients present a mild disease, 14% develop a severe condition, and 5% a critical disease that requires intensive care and mechanical ventilation. Elders and people with comorbidities, such as chronic obstructive pulmonary disease, diabetes, hypertension, and heart disease, are at higher risk of developing severe disease. In response to the pandemic, safe and effective drugs, like antivirals and monoclonal antibodies, have been searched[4].

To control this pandemic, several scientific groups around the world developed over 300 projects for the creation of vaccines. At least 40 have started the clinical phases, and 10 are in clinical phase III. The technologies used for the development of these vaccines include the use of live attenuated viruses, inactivated viruses, the use of protein S (Spike) or fragments of it; as well as DNA or mRNA platforms[5].

On December 11, the F.D.A. (Food and Drug Administration) authorized the emergency use of the BNT162b2 vaccine developed by BioNTech & Pfizer. This vaccine was included by the WHO in the emergency use catalog on December 31, 2020[6].

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The BNT162b2 is one of the vaccines applied in Mexico. It is composed of mRNA modified with nucleosides that encode the S glycoprotein of the virus, encapsulated in lipid nanoparticles[7]. In a randomized study, they observed efficacy of 95% in participants without a history of SARS-CoV-2 infection seven days after application of the second dose. This study was made in participants older than 16 years, in the United States, Argentina, Brazil, South Africa, Germany, and Turkey[8].

The main adverse reactions reported were local pain (84.1%), fatigue (62.9%), headache (55.1%), myalgias (38.2%), chills (31.9%), arthralgias (23.6%), and fever (14.2 %), mainly mild to moderate. Other severe reactions that caused the withdrawal of study patients were lymphadenopathy, shoulder injury, paroxysmal ventricular arrhythmia, and leg paresthesia[8,9].

However, little has been reported in Latin American populations although, as an emergency licensed vaccine, close monitoring of its' side effects is required. Therefore, the objective of this study was to determine the side effects in personnel vaccinated at the Military Central Hospital (H.C.M.) with the BNT162b2 vaccine.

Patients and Methods

This study was carried out in a third-level hospital in Mexico City. The population was the personnel who works within this hospital. It only included personnel who had received both doses of the BNT162b2 vaccine between December 2020 and February 2021 and agreed to participate in the study by digitally signing the informed consent. Individuals who did not correctly complete the digital survey were eliminated. This study was approved by the Research Committee of the Institution (008/2021) and attached to the guidelines of the Declaration of Helsinki.

Two groups were created, the first without history of COVID-19 and the second with a history of COVID-19. For the analysis of side effects, both groups were included, but for the determination of ANTI-SARS-CoV-2 antibodies, only participants from the first group were invited.

Through a digital survey using the Survey Monkey® platform, sociodemographic data, comorbidities, side effects, and the duration of side effects were collected.

The determination of the presence of ANTI-SARS-CoV-2 antibodies was performed using a chromatographic immunoassay, for which the Specific Serologic Test for the detection of IgG/IgM Cassette was used, (Previta – INGM-MC42 Model, Hangzhou, Zhejiang, China).

Descriptive statistics were carried out to study the population and secondary effects, and the inferential statistics used was through Chi-square using the statistical package SPSS v27.

Results

The objective of this study was to determine the frequency of side effects of the BNT162b2 vaccine in H.C.M.

The application of a two-dose schedule of the BNT126b2 vaccine is widely recommended due to its effectiveness and the low risk of severe side effects[8].

In this study, 946 people were included to determine the side effects; 62% were women (n = 592). The most frequent age range was 30-39 years of age with 44% (n = 415). Although most had not known comorbidities (80%), the most frequent comorbidity was overweight, as shown in Table I.

There were 680 participants in group 1 and 266 participants in group 2 (Table II).

After the first dose, 77% of the first group and 86% of the second group presented some side effects. After the second dose, 84% of the first group and 89% of the second group presented some side effects (Table II).

The main side effects reported in the literature are pain at the vaccination site, fatigue, headache, fever, and myalgia, similar with what was found in our study[8,10].

Table III shows the side effects. The main side effect in both doses and groups was mild pain in the application site. After the first dose, mild pain was the most frequent symptom, followed by severe pain and headache. After the second dose, they presented mild pain followed by headache and severe pain. Other reported side effects were vomiting (n = 16), lymphadenopathy (n = 12), diarrhea (n = 7), skin rash (n = 6), dyspnea (n = 6), and rhinorrhea (n = 5).

After the first dose, group 2 presented more severe pain, headache, general discomfort, myalgia, arthralgia, and chills, than group 1 (Table III). However, no significant differences were found in side effects after the second dose except for fever.

As reported in phase 1 studies of the vaccine, systemic symptoms (headache, general

Table I. Sociodemographic characteristics.

		Vaccinated (N = 946)
Age (years) n (%)	18-20	1 (0.1)
	21-29	288 (30.4)
	30-39	415 (43.9)
	40-49	222 (23.5)
	50-59	19 (0.2)
	>60	1 (0.1)
Gender n (%)	Female	592 (62.6)
	Male	354 (37.4)
Comorbidities n (%)	None	758 (80.1)
	Overweight	108 (11.4)
	Obesity	29 (3.1)
	Allergies	27 (2.9)
	Asthma	26 (2.7)
	Arterial hypertension	6 (0.6)
	Type 2 Diabetes	3 (0.3)
Previous COVID-19	Non	680 (71.8)
	Yes	266 (28.2)
Place of the previous infection n (%)	Hospital	234 (24.7)
	Home	9 (1)
	Public transport	12 (1.3)
	Other	11 (1.2)

Table II. Presence or absence of side effects after vaccination in patients with and without previous COVID-19 infection.

	First dose			Second dose		
Side effects	Group 1 n = 680	Group 2 n = 266	p (χ^2)	Group 1 n = 680	Group 2 n = 266	p (χ^2)
Present n (%)	523 (76.9)	228 (85.7)	0.003 (9.054)	568 (83.5)	236 (88.7)	0.044 (4.041)
Absent n (%)	157 (23.1)	38 (14.3)		112 (16.5)	30 (11.3)	

Table III. Side effects.

Side Effects	Dose	Group 1 n = 680	Group 2 n = 266	p (χ^2)	Vaccinated + Antibody test n = 126
Mild Pain	First	315 (46.1)	120 (45.1)	0.737 (0.113)	54 (42.9)
	Second	315 (46.3)	120 (45.1)	0.737 (0.113)	56 (44.4)
Intense Pain	First	222 (32.6)	117 (44.0)	0.001 (10.690)	53 (42.1)
	Second	208 (30.6)	90 (33.8)	0.334 (0.934)	50 (39.7)
Headache	First	185 (27)	105 (39.5)	0.0002 (13.537)	44 (34.9)
	Second	216 (31.8)	95 (35.7)	0.245 (1.352)	46 (36.5)
Fatigue	First	161 (23.7)	75 (28.2)	0.149 (2.085)	35 (27.8)
	Second	177 (26.0)	62 (23.3)	0.387 (0.750)	46 (36.5)
General Discomfort	First	126 (23.7)	84 (31.6)	0.00001 (18.853)	23 (18.3)
	Second	176 (25.9)	85 (32.0)	0.060 (3.529)	40 (31.7)
Myalgia	First	103 (15.1)	64 (24.1)	0.001 (10.449)	17 (13.5)
	Second	141 (20.7)	66 (24.8)	0.173 (1.859)	26 (20.6)
Arthralgia	First	65 (9.6)	42 (15.8)	0.007 (7.400)	12 (9.5)
	Second	103 (15.1)	48 (18.0)	0.274 (1.197)	26 (20.6)
Shivers	First	55 (8.1)	41 (15.4)	0.001 (11.252)	8 (6.3)
	Second	106 (15.6)	47 (17.7)	0.435 (0.611)	15 (11.9)
Fever	First	29 (4.3)	24 (9.0)	0.004 (8.184)	2 (1.6)
	Second	48 (7.1)	33 (12.4)	0.008 (6.983)	6 (4.8)
Numbness	First	22 (3.2)	8 (3.0)	0.857 (0.032)	5 (4)
	Second	31 (4.6)	8 (3.0)	0.281 (1.164)	7 (5.6)

Table IV. Duration of side effects.

Time (hours)	First dose		Second dose	
	Vaccinated (N = 946)	Vaccinated + Antibody test (n = 126)	Vaccinated (N = 946)	Vaccinated + Antibody test (N = 126)
Less than 24 n (%)	216 (22.8)	28 (22.2)	259 (27.4)	29 (23)
24-48 n (%)	424 (44.8)	61 (48.8)	402 (42.5)	57 (45.2)
More than 48 n (%)	69 (7.3)	8 (6.3)	68 (7.2)	12 (9.5)

malaise, fever, and other symptoms.) increased after the application of the second dose; while local symptoms (pain at the vaccination site) remain similar in both[8] which concurs with our results. These findings might be due to the second dose of the vaccine causing a more intense activation of the immune system, leading to the production of pro-inflammatory cytokines, therefore leading to systemic and local manifestations[10].

Within our results, we identified that patients without a history of COVID-19 presented fewer side effects in the first dose than patients with previous SARS-CoV-2 infection. Angyal et al[11] suggest that the specific response of T cells towards protein S is higher in people with previous infection relative to those who do not have a history of COVID-19; nevertheless, this response is paired with two doses of the vaccine in people with no history. The reaction to vaccination of people with previous SARS-CoV-2 infection can generate new responses against non-recognized regions of protein S during infection, and thus enhance responses towards previously recognized epitopes whose titles were below detection levels[11]. This may explain the increased frequency of side effects after the first dose in people with history of COVID-19 compared to those without previous infection. After the second dose, the side effects were similar in both groups; since there is already a response by the T cells in people with or without a history of infection.

Duration of symptoms was analyzed finding that regardless of the history of previous infection or the dose received, almost 50% of the patients remitted their symptoms within 24-48 hours (Table IV).

The presence of IgG and IgM anti-SARS-CoV-2 was detected in 126 participants of this subgroup, predominantly conformed by women (77%), the most frequent age range was between 30 to 39 (46%), the most common comorbidity was overweight (18.3%). The side effects presented were similar to those presented by group 1 (Table III). In a range of 24 to 48 hours after the vaccination, the symptoms were mainly remitted (Table IV).

All 126 participants were IgG positive, only 26.9% of them were IgM positive. The time between second dose vaccination and the collection of samples for patients with positive IgG was a median of 18 days (13 days, 21 days), and those with IgM positives were 17.5 days (12.8 days, 20.3 days).

The low percentage of people with positive IgM may be due to the fact that the sample was taken 17.5 days after the second dose, according to what has been reported, the maximum peaks are at 21 days after the first dose or at seven days after the second, so it was unlikely to find positive levels of IgM[12].

Conclusions

Our results match with other reported literature. The most common side effects were pain in the vaccination site, headache, fatigue, and general discomfort, these being well-tolerated and remitting between 24 to 48 hours. In addition, a positive correlation was identified between the existence of side effects after the first dose in patients with a history of previous SARS-CoV-2 infection, compared to those who did not. However, this correlation is not present after the second dose. Finally, it was found that the IgM absence can be related to the interval between the vaccination and the sample collection.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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