COVID-19 Vaccine and Fitness to Fly

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INTRODUCTION: On December 2020 the U.S. Food and Drug Administration (FDA) authorized the emergency use of Pfizer-BioNTech COVID-19 vaccine. This new vaccine has several side effects that can potentially impair function, which warrants special attention regarding aircrews' fitness to fly following vaccination.
 METHODS: A survey was conducted in the Israeli Air Force (IAF) Aeromedical Center in order to characterize the side effects and their duration following Pfizer-BioNTech COVID-19 vaccine administration to aviators.
 RESULTS: The most common side effect was injection site pain. Headache, chills, myalgia, fatigue, and weakness were more common following the second dose administration. The difference is statistically significant. Following the second vaccine, duration of side effects was longer compared to the first vaccine (*P*-value = 0.002).
 CONCLUSION: The IAF Aeromedical center policy for Pfizer-BioNTech COVID-19 vaccine recipients among aircrew members, based on side effects duration and severity, is to temporarily ground from flight duties for 24 and 48 h following the first and the second dose, respectively.

KEYWORDS: COVID-19 vaccine, aircrew, aviation, corona virus, side effects, aeromedical waiver.

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The coronavirus disease 2019 (COVID-19) outbreak in late 2019 brought the world to a standstill.^{3,6,16} The clinical manifestations of the disease caused by the novel severe acute respiratory syndrome associated with coronavirus 2 (SARS-CoV-2) may include cardiac, pulmonary, and coagulation disorders,^{9,10,12} as well as psychosocial issues that can impair recovered aviators' fitness to fly. Although most of the infected IAF aircrew members were mildly affected, there are reports about subtle manifestations that can result in unexpected deterioration during flight. Therefore, a post-recovery workup was suggested in the Israeli Air Force Aeromedical Center in order to rule out complications that can impact aircrew members.⁸

Since the outbreak began, researchers around the world have been racing to develop COVID-19 vaccines, with at least 166 vaccines currently in preclinical and clinical development.¹⁷ During that period, a novel mechanism of a lipid nanoparticle-encapsulated messenger ribo-nucleic acid (mRNA) that encodes the full-length spike protein of the SARS-CoV-2 was developed.² On December 2020 the U.S. Food and Drug Administration (FDA) authorized the emergency use of two mRNA vaccines produced by Pfizer-BioNTech and Moderna.^{4,11} Since then, significant efforts have been made by the Israeli Ministry of Health, who launched the "Back to Life" campaign in order to vaccinate most of the Israeli population. As part of those efforts, an Israel Defense Forces Medical Corps vaccination program has been initiated, aiming to inoculate Israeli Defense Force service members, as they are critical for state security and defense. A part of this program is the vaccination of aircrew members in the Israeli Air Force (IAF).

In an ongoing clinical trial, the Pfizer-BioNTech COVID-19 vaccine was proven effective in preventing SARS-CoV-2 following two doses given 3 wk apart. The duration of protection against COVID-19 is currently unknown but expected to be at least 6 mo.²

Many side effects have been associated with the Pfizer-BioNTech COVID-19 vaccine, including injection site pain, fatigue, headaches, myalgia, chills, arthralgia, fever, nausea, and swollen lymph nodes. In rare cases, a severe allergic reaction

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has been reported after receiving the Pfizer-BioNTech COVID-19 vaccine. 15

Even though the most commonly reported side effect was pain at the injection site, other systemic side effects can affect the fitness of the vaccinated individual.⁷ Systemic events were reported more often by younger vaccine recipients (18 to 65 yr of age)⁵ and more often following the second dose of the vaccine. Fatigue and headache were the most commonly reported systemic events. Fever above 38°C was reported by 16% of the younger recipients compared with 11% of the older recipients (\geq 65 yr of age).

As observed among vaccinated persons demonstrating local side effects that were mild to moderate and lasted 24–48 h, systemic side effects (especially chills and fever) were also reported during the first 2 d. In order to maintain the highest level of safety and as recommended by the U.S. Federal Aviation Administration,¹⁴ the IAF aeromedical center determined a post-vaccination observation period for aircrew members lasting 48 h until further notice.

According to U.S. Air Force,¹ following vaccination, access to medical care on the ground is recommended for a period of 4 h and no aeromedical waiver is required. It is customary that aircrew members in the IAF are grounded for 12 h following most vaccines. Unlike the other vaccines that are known to be safe and with short-term side effects, Pfizer-BioNTech COVID-19 vaccine required special consideration due to its side effects profile and its recent approval.

Reports describing increased severity and duration of systemic side effects following the second vaccine dose in comparison to the first dose led to this study. Our goal was to assess the amount and extent of side effects in our aircrew members. We hypothesized that side effects will be more common and severe following the second vaccine dose.

METHODS

Israeli Air Force aircrew members who were vaccinated between December 2020 to February 2021 with the first and second dose of Pfizer-BioNTech COVID-19 vaccine participated in our research. A short survey, conducted by the Israeli Air Force Aeromedical Center, was sent 1 wk following each dose to the vaccinated aircrew members.

Participants were asked about a variety of side effects, including local injection site pain, swelling and redness, headache, fever above 38°C, chills, myalgia, arthralgia, allergic reaction (local or systemic), dyspnea, fatigue, general weakness, facial numbness, nausea, diarrhea, or none of the above. A positive answer to any of the above questions required the participant to describe the duration of the side effect (0–24, 24–48, 48–78 h, or other). Questions were asked about first and second doses separately.

Nonparametric tests for two related samples were used in order to compare the difference between the first and the second dose. We used McNemar and Wilcoxon tests to compare nominal and ordinal variables respectively. Statistics were analyzed using Statistical Package for the Social Sciences (SPSS) software (version 21; IBM, Armonk, NY, USA). Ethical approval was received by the Israel Defense Forces Institutional Review Board committee.

RESULTS

A total of 127 aircrew members answered the survey until February 21st, 2021. All of them received both doses of the Pfizer-BioNTech COVID-19 vaccine. Overall, the survey response rate was 33.6%. Male aircrew response rate was 34% and female 63%. Response rate was 24% and 43% for high and low performance aircrew members, respectively. Junior aircrew members' response rate (Lieutenant and Captain) was 38%, whereas seniors' rate (Major and higher) was 31%.

Table I describes participant's characteristics and the general distribution of side effects. The average age was 33 (range 21–53). Most of the participants were helicopter aircrew members (54%), while the other were combat (29.9%) and transport (27.6%) aircrew members. Following the first dose, 85.8% of participants reported experiencing side effects, whereas 94.5% reported side effects following the second dose. There was no significant difference between aircraft platform members (combat, transport, and helicopter aircraft) regarding side effects.

The most common side effect was injection site pain, reported by 82.7% of aircrew members following the first dose and by 79.5% following the second dose (**Table II**). The total number of local side effects reported following the first and second dose was similar with no statistically significant difference.

Table I. Participants' Characteristics.

VARIABLE	N (%) (N = 127 TOTAL)		
Age			
Mean	33.29		
Standard deviation	8.385		
Range	21–53		
Aircraft platform			
Combat	38 (29.9%)		
Transport	35 (27.6%)		
Helicopter	54 (42.5%)		
Side effects			
First dose			
Yes	109 (85.8%)		
No	18 (14.2%)		
Second dose			
Yes	120 (94.5%)		
No	7 (5.5%)		
Duration of side effects			
First dose			
0–24 h	61 (58.1%)		
24–48 h	41 (39%)		
48–72 h	2 (1.9%)		
>72 h	1 (1%)		
Second dose			
0–24 h	56 (48.7%)		
24–48 h	53 (46.1%)		
48–72 h	5 (4.3%)		
>72 h	1 (0.9%)		

 Table II.
 Side Effects Comparison Between the First and Second Dose of the Vaccine.

		SECOND	
	FIRST DOSE	DOSE	_
SIDE EFFECT	N (%)	N (%)	P-VALUE
Local			
Injection site pain	105 (82.7)	101 (79.5)	0.55
Swelling	2 (1.6)	2 (1.6)	1
Redness	0 (0)	1 (0.8)	1
Allergic reaction	0 (0)	0 (0)	
(pruritus, rash)			
Systemic			
Headache	6 (4.7)	38 (29.9)	< 0.005
Fever	0 (0)	7 (5.5)	0.16
Chills	0 (0)	17 (13.4)	< 0.005
Myalgia	4 (3.1)	22 (17.3)	< 0.005
Arthralgia	0 (0)	4 (3.1)	0.125
Systemic allergic reaction	0 (0)	1 (0.8)	1
Fatigue	4 (3.1)	50 (39.4)	< 0.005
General weakness	7 (5.5)	49 (38.6)	< 0.005
Facial numbness	0 (0)	1 (0.8)	1
Vomiting	0 (0)	1 (0.8)	1

The total number of side effects per participant, and especially systemic ones, were more common following the second vaccine (*P*-value < 0.005). Headaches were reported by 4.7% following the first dose, which increased by ninefold to 38% following the second dose (*P*-value < 0.005). A few participants described other systemic side effects following the first vaccine, including myalgia (3.1%), general weakness (5.5%), and fatigue (3.1%). However, following the second vaccine, 39.4% reported fatigue, 38.6% reported general weakness, 13.4% suffered from chills, and 17.3% from myalgia. The proportional differences between the first and the second vaccine was statistically significant for all these side effects.

As described in **Fig. 1**, following the first vaccine, 58.1% of aircrew members suffered from side effects during the first 24 h following vaccination, while only 39% reported such side effects on the following day (24–48 h). Among the recipients of the second vaccine, the reporting distribution is almost equal between the first day and the second day (48.7% and 46.1%). Only a few participants reported side effects between 48–72 h and above. The longer duration of side effects following the second dose was higher and found to be statistically significant compared to the first vaccine administration (*P*-value = 0.002).



Fig. 1. Side effects duration following first and second vaccine doses.

The Israeli Air Force aeromedical waiver is mandatory for any medical issue of aircrew members, especially following the use of recently approved medical technologies. Thus, the recent FDA authorization required appropriate precautions following the vaccination of aircrew members. Although vaccines are one of the greatest public health achievements of the last century, their administration is commonly followed by a variety of adverse events. These reactions indicate physiological immune responses that are critical for the development of acquired immunity.¹³

Unlike other vaccines, which routinely ground from flying duties for 12 h (unless symptoms persist), the described side effects, and especially their duration following Pfizer-BioNTech COVID-19 vaccine, require special consideration regarding flying fitness. Some of the side effects reported by the literature and our survey (including severe injection site pain, headaches, myalgia, weakness, and fatigue) may cause significant discomfort while flying, impair aviator's performance, and even possibly result in sudden incapacitation. For example, a combination of fever and dehydration with hemodynamic changes may lead to low G tolerance in high performance aircrafts. As previously described, a significant portion of our participants experienced these systemic side effects, especially following the second dose.

Side effect duration is a very important factor when debating the decision regarding grounding period. Most participants who received the first dose suffered from side effects during the first 24 h. A more significant proportion of participants described side effects following the second dose during the second day (24–48 h). Although some have reported side effects lasting up to 72 h and above, it was a minor part of the tested population.

The differences between reported side effects following first and second vaccine doses led to the decision on different grounding time intervals for vaccinated aircrew members. Due to the very minor proportion of described systemic side effects following the first vaccine, we decided on 24 h of observation before return to flying duties. However, a period of 48 h of medical observation following the administration of the second vaccine is needed in order to maintain the highest level of safety among aircrew members. Due to the lack of difference in side effect reporting, we decided not to differentiate between the flight platforms and the number of crewmembers.

The main limitation of our survey seems to be information bias. In order to preserve their flying fitness, aircrew members may submit an incomplete report regarding their medical issues. Given the similarity between the reports in the literature and the reports in our survey, we assume that the bias is minimal.

Due to the difference between survey response rates, selection bias likely occurred in our research. Although low performance and female aircrew members had a higher response rate, the relative amount of them is low. Thus, any minor change could significantly affect the response rate. Moreover, we have not found a biological explanation in the literature that would explain the difference in side effects between aircrew member subgroups. We believe our survey adequately represents our aircrew population.

In conclusion, our survey demonstrated systemic side effects with longer duration following the second vaccine administration compared to the first one. Our findings support the IAF Aeromedical Center policy for aircrews vaccinated with the Pfizer-BioNTech COVID-19 vaccine. Limitation for duties not involving flight for 24 and 48 h following the first and the second dose, respectively, seems to be safe and effective policy.

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REFERENCES

- Approved air force aerospace medicine approved medications. [Accessed February 2021]. Available from: https://www.315aw.afrc.af.mil/Portals/ 13/Medical/Aircrew%20Med%20List%2013%20May%202019.pdf? ver=2019-05-14-121706-100.
- Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. N Engl J Med. 2021; 384 (5):403–416.
- Centers for Disease Control and Prevention. 2019 novel coronavirus, Wuhan, China. Information for healthcare professionals. [Accessed February 2021]. Available from https://www.cdc.gov/coronavirus/2019nCoV/hcp/index.html.
- 4. Emergency Use Authorization (EUA) of the Pfizer-BioNTech COVID-19 vaccine to prevent coronavirus. Fact sheet for healthcare providers

administering vaccine. [Accessed February 2021]. Available from https://www.fda.gov/media/144413/download.

- Food and Drug Administration. Briefing document. Pfizer-BioNTech COVID-19 vaccine. Vaccines and Related Biological Products Advisory Committee Meeting. December 10, 2020. [Accessed February 2021]. Available from https://www.fda.gov/media/144245/download.
- Gandhi RT, Lynch JB, Del Rio C. Mild or moderate COVID-19. N Engl J Med. 2020; 383(18):1757–1766.
- Gee J, Marquez P, Su J, Calvert GM, Liu R, et al. First month of COVID-19 vaccine safety monitoring - United States, December 14, 2020–January 13, 2021. MMWR Morb Mortal Wkly Rep. 2021; 70(8):283–288.
- Gilad D, Gabbai D, Tehori O, Nakdimon I, Bar-Shai A, et al. Return to aviation duty following recovery from COVID-19. Journal of Military, Veteran and Family Health. 2021; 7(2):116–120.
- Guan WJ, Zhong NS. Clinical characteristics of COVID-19 in China. [Reply]. N Engl J Med. 2020; 382(19):1861–1862.
- Huang C, Wang Y, Li X, Ren L, Zhao J, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020; 395(10223):497–506.
- Jackson LA, Anderson EJ, Rouphael NG, Roberts PC, Makhene M, et al. An mRNA vaccine against SARS-CoV-2 - preliminary report. N Engl J Med. 2020; 383(20):1920–1931.
- 12. Lai CC, Ko WC, Lee PI, Jean SS, Hsueh PR. Extra-respiratory manifestations of COVID-19. Int J Antimicrob Agents. 2020; 56(2):106024.
- Nakayama T. Causal relationship between immunological responses and adverse reactions following vaccination. Vaccine. 2019; 37(2):366–371.
- Novel coronavirus (COVID-19) Update. [Accessed February 2021]. Available from https://www.faa.gov/news/updates/?newsId=94991.
- Shimabukuro T, Nair N. Allergic reactions including anaphylaxis after receipt of the first dose of Pfizer-BioNTech COVID-19 vaccine. JAMA. 2021;325(8):780–781.
- World Health Organization. Director-General's remarks at the media briefing on 2019-nCoV on 11 February 2020. [Accessed February 2021]. Available from http://www.who.int/dg/speeches/detail/who-directorgeneral-s-remarks-at-the-media-briefing-on-2019-ncov-on-11february-2020.
- World Health Organization. Draft landscape of COVID-19 candidate vaccines. [Accessed February 2021]. Available from https://www.who.int/ publications/m/item/draft-landscape-of-covid-19-candidate-vaccines.