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TO VACCINATE OR NOT TO VACCINATE – BNT162b2 SEROCONVERSION RATE AND SIDE EFFECTS AMONG POLISH HEALTHCARE WORKERS

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Abstract
Objectives: The study aimed to analyze the effect of BNT162b2 vaccination among Polish healthcare workers in terms of serologic response and adverse events. **Material and Methods:** A questionnaire survey covered data in the period January 1–March 31, 2021 gathered in 2 hospitals in Wielkopolska, Poland. Additionally, serological analysis (SARS-CoV-2 anti-S protein IgG) was performed. **Results:** A total of 617 medical workers were vaccinated with BNT162b2 (Comirnaty, Pfizer). Data from the questionnaires were received from all of the staff after the first and the second dose. No severe side effects were observed. The most common side effect following the first and second doses of vaccination was pain at the injection site. After the first dose, 3 (1.4 %) women aged 18–55 years, 5 women (3.9 %), and 3 men (8.3 %) aged >55 years had negative SARS-CoV-2 anti-S protein IgG result. After the second dose, all those who agreed to have antibodies tested responded to vaccination with positive SARS-CoV-2 anti-S protein IgG results. **Conclusions:** Vaccination tolerance was good in the studied population; no severe side effects were observed. After the second dose, all tested healthcare workers responded to vaccination with antibody production. Int J Occup Med Environ Health. 2022;35(6)

Key words:
vaccination, healthcare, side effect, COVID-19, SARS-CoV-2, BNT162b2

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INTRODUCTION

Vaccinations are considered to be one of the most outstanding achievements of modern medicine. Their use has significantly contributed to the control of dangerous epidemics of infectious diseases. In 1796, Dr. Edward Jenner developed the first vaccine, protecting against smallpox infection. Since then, vaccines have become the central pillar of prophylaxis in medicine [1]. Mass vaccinations against SARS-CoV-2 seem one of the ways to end the pandemic that started in March 2020.

Since the beginning of the pandemic, many medical companies have started working on vaccine candidates using different approaches. The U.S. Food and Drug Administration (FDA) on December 11, 2020 issued an Emergency Use Authorization (EUA) for the Pfizer-BioNTech COVID-19 (BNT162b2) vaccine – nucleoside-modified mRNA vaccine encoding the spike glycoprotein of SARS-CoV-2 [2]. COVID-19 vaccines are developed following the exact legal requirements and safety standards as for all other medications. Once an effective vaccine is developed, it is crucial that there is equitable access and distribution of vaccines to protect the public's health. Due to the lack of vaccines, the prioritization must be carried out at the national level. The group in the highest need of protection are healthcare workers [3]. Most European Union (EU) countries have developed strategies for the deployment of the COVID-19 vaccine in which healthcare workers are a priority group.

In Poland, the vaccination process among "group 0" (healthcare workers) started on December 26, 2020, and was crucial for the national healthcare system. In the first weeks of 2021, a large percentage of healthcare workers were offered vaccinations against COVID-19. The conducted study is the first to show the effect of BNT162b2 vaccination among Polish residents.

MATERIAL AND METHODS

A paper-based questionnaire survey was conducted. Data were collected from medical workers (doctors, nurses, physiotherapists, laboratory diagnosticians, cleaning, logistics, and administrative staff together with retired employees) from 2 hospitals in Wielkopolska, Poland. These are 2 from 54 hospitals in the region where all of the team without contraindications was vaccinated with Comirnaty (Pfizer). The vaccines were provided by the government free of charge. All of the people were vaccinated in the first quarter of 2021.

The questionnaire consisted of 2 parts: demographic and medical. In the demographic part, the respondents were to provide their primary data (including age) and the date of vaccination. In the medical aspect, they answered questions about side effects from a set of prepared answers such as fever, allergic reaction, fatigue, muscle pain, pain at the injection site, reaction at the site of the injection. There was also space to enter any additional symptoms if any occurred. Questionnaires were collected 2 weeks after vaccination (respondents had 14 days to check their signs). What is more, response to vaccination based on the production of IgG antibodies against the SARS-CoV-2 S protein (Elecsys® Anti-SARS-CoV-2, qualitative, specific for Receptor Binding Domain test, Roche Diagnostics) was measured 3 weeks after the first dose and 2 weeks after the second dose. Finally, the COVID-19 disease status was also checked (asking during anamnesis about positive SARS-CoV-2 PCR test in the past).

The consent for this study was given by the Bioethics Committee at the Poznan University of Medical Sciences, Poznań, Poland.

Statistical analysis was performed using PQStat 1.8.2.142 (PQStatSoftware). A χ^2 test was used to compare nominal data. The significance was set at the level of $p < 0.05$.

RESULTS

In the period of January 1–March 31, 2021, 617 medical workers were vaccinated with Comirnaty (Pfizer, New York, USA). Data from the questionnaires were received from all of the staff after the first and the second dose.

Table 1. Adverse events analysis after Comirnaty (Pfizer) vaccination among medical workers, January 1–March 31, 2021, Poznań and Słupca (Poland)

Adverse event	Participants (N = 617) [n (%)]							
	1st dose				2nd dose			
	women (N = 520)		men (N = 97)		women (N = 520)		men (N = 97)	
	18–55 years	>55 years	18–55 years	>55 years	18–55 years	>55 years	18–55 years	>55 years
Fever	12 (3.6)	6 (3.3)	3 (6.4)	2 (4.0)	51 (15.2)	16 (8.7)	5 (10.6)	5 (10.0)
38.0–39.0°C	12 (3.6)	6 (3.3)	2 (4.3)	2 (4.0)	40 (11.9)	12 (6.5)	5 (10.6)	4 (8.0)
39.1–40.0°C	0	0	1 (2.1)	0	10 (3.0)	4 (2.2)	0	1 (2.0)
>40.0°C	0	0	0	0	1 (0.3)	0	0	0
Allergic reaction	4 (1.2)	4 (2.2)	0	0	12 (3.6)	1 (0.5)	1 (2.1)	1 (2.0)
Fatigue	80 (23.8)	24 (13.0)	11 (23.4)	3 (6.0)	146 (43.5)	48 (26.1)	11 (23.4)	13 (26.0)
<24 h	42 (12.5)	16 (8.7)	7 (14.9)	2 (4.0)	88 (26.2)	30 (16.3)	7 (14.9)	9 (18.0)
24–48 h	30 (8.9)	7 (3.8)	3 (6.4)	1 (2.0)	42 (12.5)	11 (6.0)	3 (6.4)	4 (8.0)
49–72 h	5 (1.5)	1 (0.5)	0	0	11 (3.3)	3 (1.6)	1 (2.1)	0
>72 h	3 (0.9)	0	1 (2.1)	0	5 (1.5)	4 (2.2)	0	0
Muscle pain	77 (22.9)	22 (12.0)	5 (10.6)	3 (6.0)	102 (30.4)	36 (19.6)	9 (19.1)	14 (28.0)
<24 h	45 (13.4)	16 (8.7)	3 (6.4)	3 (6.0)	61 (18.2)	26 (14.1)	4 (8.5)	9 (18.0)
24–48 h	25 (7.4)	4 (2.2)	2 (4.3)	0	32 (9.5)	7 (3.8)	5 (10.6)	5 (10.0)
49–72 h	6 (1.8)	2 (1.1)	0	0	8 (2.4)	1 (0.5)	0	0
>72 h	1 (0.3)	0	0	0	1 (0.3)	2 (1.1)	0	0
Pain at the injection site	240 (71.4)	111 (60.3)	34 (72.3)	26 (52.0)	202 (60.1)	104 (56.5)	25 (53.2)	12 (24.0)
<24 h	123 (36.6)	72 (39.1)	20 (42.6)	22 (44.0)	121 (36.0)	71 (38.6)	19 (40.4)	6 (12.0)
24–48 h	82 (24.4)	27 (14.7)	11 (23.4)	3 (6.0)	59 (17.6)	22 (12.0)	6 (12.8)	4 (8.0)
49–72 h	30 (8.9)	12 (6.5)	3 (6.4)	0	17 (5.1)	5 (2.7)	0	0
>72 h	5 (1.5)	0	0	1 (2.0)	5 (1.5)	6 (3.3)	0	2 (4.0)
Reaction at the injection site	13 (3.9)	12 (6.5)	1 (2.1)	0	21 (6.3)	12 (6.5)	0	1 (2.0)
<5 cm	12 (3.6)	10 (5.4)	0	0	13 (3.9)	8 (4.3)	0	1 (2.0)
≥5 cm	1 (0.3)	2 (1.1)	1 (2.1)	0	8 (2.4)	4 (2.2)	0	0
Other	63 (18.8)	20 (10.9)	5 (10.6)	1 (2.0)	116 (34.5)	29 (15.8)	8 (17.0)	2 (4.0)

In the study group, women predominated (N = 520, 84%), and the median age in the entire group was 51 years (18–90 years).

Adverse events are presented in Table 1. Symptoms of an allergic reaction were: lacrimation, rhinitis, Quincke's edema, rash. No anaphylactic shock was observed in the study group. Reaction at the injection site was redness and swelling. Other adverse reactions cited by respondents included: headache, abdominal pain, diarrhea, vomiting, nausea, vertigo, enlargement of regional lymph nodes, paralysis of the brachial plexus on the injection site (2 patients), torticollis on the injection site (1 patient). All of them fully recovered.

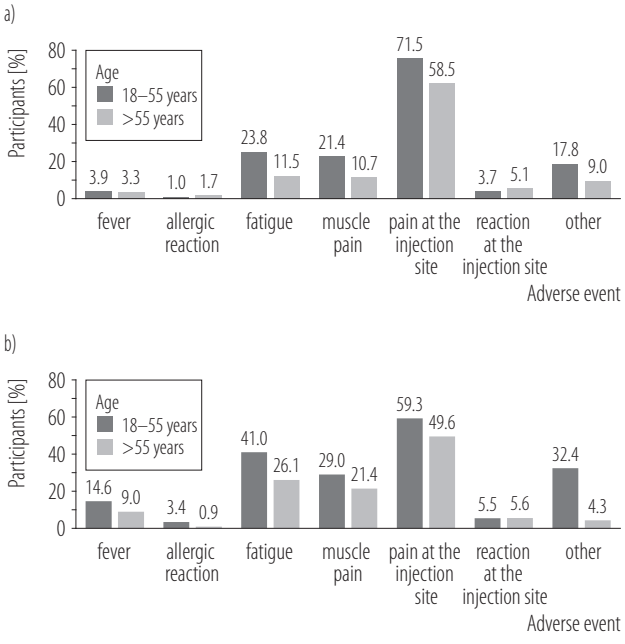

Figure 1. Adverse events after a) the 1st and b) the 2nd vaccine dose of Comirnaty (Pfizer) vaccination among medical workers (N = 617), January 1–March 31, 2021, Poznań and Słupca (Poland)

More adverse reactions were observed after the second dose than after the first one ($p < 0.01$). However, the most common adverse event reported in every group – pain at the injection site – was more common after the first dose ($p < 0.01$) (Figure 1). Local reactions in the form of increased redness and/or swelling at the injection site were observed more often after the second dose ($p < 0.01$). The most minor reported reactions were allergic ones. The respondents reported generalized reactions such as muscle pain and fatigue. They were also more common after the second dose ($p < 0.01$) (Figure 1).

Between the first and the second vaccine dose, 6 people were infected with SARS-CoV-2 – the result was confirmed with PCR test. All of them were healthy participants (without comorbidities), did not require hospitalization, only symptomatic outpatient treatment.

They were vaccinated later with the double dose according to the vaccination rules, so their questionnaires were also included.

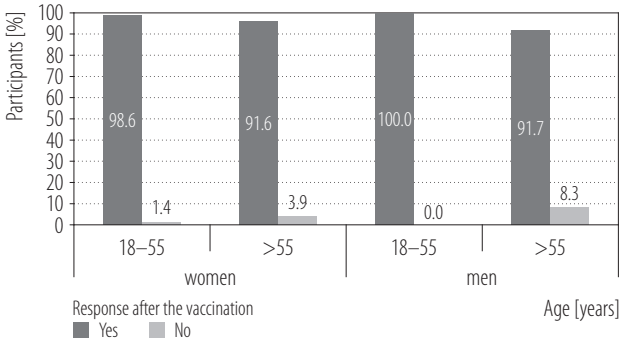

Figure 2. Response after the first dose among women and men of Comirnaty (Pfizer) vaccination among medical workers (N = 617), January 1–March 31, 2021, Poznań and Słupca (Poland)

The serologic response was tested after the first and the second dose (Figure 2).

After the first dose, 419 people agreed to be tested. Among women aged 18–55 years old, 3 (1.4 %) did not respond to the vaccine (had negative SARS-CoV-2 anti-S protein IgG result).

After the second dose, all those who agreed to have antibodies tested responded to vaccination (384 people) with positive SARS-CoV-2 anti-S protein IgG results. This group also included patients who did not respond positively after the first dose of the vaccine.

DISCUSSION

In the studied population, the overall vaccination tolerance was good. No severe side effects were observed after the first or second dose of the vaccine. This is in line with the literature data [4]. In the study performed by Mulligan et al. [4], the vaccine at 1 out of 3 doses (10 μg, 30 μg, and 100 μg) was given to 36 healthy adults (age range 18–55 years), with 9 other participants receiving a placebo treatment. The participants in all but the highest dosage groups (100 μg and 60 μg, respectively) received 2 vaccinations at 3-week intervals. After the second dose, the pain was reported by 83.3% and 100.0% of individuals who received 10 μg and 30 μg BNT162b1, respectively.

All local reactions were mild or moderate in severity except for one report of severe pain after the first dose of 100 μg BNT162b [4].

In the study performed by Sahin et al. [5], injection site reactions involved pain and tenderness; reactogenicity was dose-dependent and was more pronounced after the booster dose. The associated symptomatology, such as fever, chills, headache, muscle pain, joint pain, injection site pain, and tenderness, was primarily mild or moderate, with occasional severe (grade 3) manifestations. In the 30-microgram dose level cohort, 2 out of 12 (16.7%) subjects experienced severe local reactogenicity; 6 out of 12 (50%) subjects reported severe systemic reactogenicity (primarily headache, chills, fatigue, or muscle pain); and 1 subject out of 12 (8.3%) reported fever. These adverse events were transient, resolved spontaneously, and increased after the booster immunization. In our group, the most common side effect following the first and second doses of Comirnaty was pain at the injection site. Percentages observed in our group are lower compared to the data from Mulligan et al. [4] and Sahin et al. [5]. This can be explained by the fact that our group is comprised of healthcare workers, who are a particular group of patients. They may have a higher tolerance to minor discomfort. This might be an explanation why pain at the injection site was reported less often after the second dose (65% vs. 54%).

Paralysis of the brachial plexus (2 people) on the injection site and torticollis (1 person) on the injection site was considered the most serious side effect. They were associated with the first dose (1 case of paralysis of brachial plexus and the case of torticolitis); however, the patients did not refuse a subsequent dose of Comirnaty.

The systemic reactogenicity observed more often in the younger group is caused by the direct action of the vaccine. Upon entry to the cell, the mRNA induces an innate reaction [6]. This leads to interferon production. Interferon acts locally on surrounding cells – making them ready to respond to antigen stimuli. mRNA acts as an adjuvant in this vaccine. The clinical symptoms of interferon action are fever, chills, fatigue, myalgia, arthralgia, nausea, and lethargy. After synthesis, the spike protein is displayed on the cell surface and causes the immune system to produce antibodies and activate T lymphocytes, which eliminate from the body cells presenting foreign antigens at the injection site. This can cause the symptoms mentioned above.

Systemic reactogenicity was more frequent and severe after the second dose of vaccination, regardless of the patients' age. However, the symptoms were transient and resolved within a few days. After the first dose of Comirnaty, side effects were reported more frequently in the group of younger people up to 55 years of age except from allergic reaction and injection site reaction, both of which were more commonly reported in patients >55 years of age. However, after the second dose, all vaccine effects were more pronounced in the younger group (e.g., 3.65% vs. 11.8% fever reports, 17.65% vs. 33.55% fatigue reports). In the clinical trial, systemic events increased with the dose level and were reported in a greater number of participants after the second dose [4]. This is probably related to the deterioration of the body's immune response, both humoral and cellular, with age.

In the study group, after the administration of the first dose of vaccination, a more robust immune response (positive SARS-CoV-2 anti-S protein IgG result) was noted in younger people, which is consistent with the published studies. In the 18–55 age group, the response to the vaccine was 100% in the male group and 98.6% in the female group. However, among people aged >55, 5 (3.9%) women and 3 (8.3%) men did not respond.

Nevertheless, all those who agreed to have antibodies tested after the second dose responded to vaccination (384 out of 419 people) with positive SARS-CoV-2 anti-S protein IgG levels. The recorded immune responses show that mRNA vaccines are very promising.

The findings of this study have to be interpreted in light of several limitations. First, the one-time follow-up took place only 14 days after the second dose of the vaccine. Due to the limited number of days following the second dose of the vaccine, both adverse effects and positive SARS-CoV-2 PCR tests beyond this time remain unknown. Moreover, out of 617 fully vaccinated people, the number of people who agreed to be tested for the production of SARS-CoV-2 anti-S protein IgG after the first and second dose amounted to merely 419 after the first dose and 384 after the second dose. Another constraint is that we did not perform T cell analysis to monitor cellular response. In further studies, it would be relevant to determine whether vaccinations are effective in preventing asymptomatic infections or disease transmission. This would be of the most significant importance for the healthcare workers with heavy exposure to the SARS-CoV-2. The humoral response is only one part of the immune response to vaccines. To date, there has been published at least one study focusing on this issue [7].

CONCLUSIONS

Younger healthcare workers were more likely to experience side effects. The most common were local symptoms. Significantly more post-vaccination complications were observed after the second dose, especially the systemic ones. After the second dose, all patients had antibodies against SARS-CoV-2. The obtained results may provide a good argument for society as a whole to decide to vaccinate against COVID-19 and therefore help to achieve herd immunity.

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