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Safety of mRNA COVID-19 vaccinations in patients with allergic diseases

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A B S T R A C T

Objectives: The aim of this study was to determine the degree of safety and possible risk of acute allergic reactions following mRNA COVID-19 vaccination among a group of patients predisposed to allergic diseases.

Study design: The study survey took place between May 2021 and February 2022. Each participant completed an initial pre-vaccination questionnaire during patient eligibility assessment for vaccination, and two subsequent questionnaires were completed approximately 21 days after the first and second doses of vaccination.

Methods: The study included 52 patients aged >18 years. Participants were a select group of patients who, due to a history of severe allergic disease, were not eligible for vaccination at the COVID-19 Vaccination Points available in Poland.

Results: None of the patients developed serious allergic complications in the form of anaphylaxis. There were no statistically significant differences between the first vaccination and the second vaccination in terms of symptoms, the time of onset and duration. The age of the participants did not correlate statistically with the occurrence of symptoms following the first or second vaccination.

Conclusions: Based on the study results, it can be concluded that mRNA COVID-19 vaccines show a favourable safety profile for patients with a history of allergic disease and constitute the optimal strategy for fighting the SARS-CoV-2 pandemic. The study results support the recommendation of COVID-19 vaccinations for people predisposed to allergic diseases due to the clear benefits of vaccination over the possible risk of adverse events.

1. Introduction

Since December 2019, SARS-CoV-2, the virus that causes COVID-19, has resulted in over 491 million cases and 6.15 million deaths worldwide [1,2]. The SARS-CoV-2 virus created new problems and resulted in the rapid development of research on innovative methods to protect against the disease and severe course of COVID-19. Pre-pandemic, research on mRNA vaccines was limited to theoretical considerations and small clinical trials. However, the COVID-19 pandemic created an urgent global vaccination requirement and substantial research funding was made available, which enabled the creation of mRNA vaccinations to protect the entire human population. The COVID-19 pandemic has undoubtedly strengthened the role of vaccinations and is undoubtedly one of the greatest achievements in medicine.

COVID-19 is most frequently transmitted through droplets. This virus shows the highest affinity to the respiratory epithelial cells of the lower respiratory tract because of its necessity to bind to the membrane receptor for angiotensin-converting enzyme 2 (ACE2). The membrane receptor for ACE2 is the binding site of the receptor-binding domain (RBD) domain within the S1 protein of the virus, and this connection, through the cycle of conformational changes involving the S2 protein, allows the virus to enter the cell [3–6].

The genetic material of the virus is released in the cytosol - a single strand of positive ssRNA polarity (+). After the translation of basic proteins, a reverse transcription complex (RCT) forms on the host ribosomes, where the viral genetic material is multiplied. Within the viral RNA, non-structural (necessary for replication), structural and auxiliary proteins are encoded [7,8].

After COVID-19 infection, specific immunoglobulins against the S1 protein and N protein, encoded within the genetic material of the virus, are produced; however, after mRNA vaccination, the antibodies against the N protein are absent, as the mRNA of the vaccine does not contain the N protein gene. The genetic vaccines available on the market (Pfizer, Moderna) contain mRNA encoding only the S protein; thus, vaccinated individuals only produce S-protein-specific antibodies [9,10].

All mRNA vaccines used so far have been administered

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intramuscularly. Shortly after the injection, bulks of lipid nanoparticles (LNP)-mRNA enter the muscle cells by endocytosis and the mRNA is translated and the S protein is formed. Next, the network of blood vessels adjacent to the muscles can recruit infiltrating antigen presenting cells (APCs). In the case of mRNA vaccines designed with full-length S protein, the translation product contains a signal peptide from amino acids 1 to 15, which allows the transport of the S protein to plasma membranes or secretion from the cytoplasm. Meanwhile, most of the protein is degraded in the endosome derived proteasome and is then incorporated as a part of the major histocompatibility complex class I (MHC) and will be presented to $CD8^+$ and $CD4^+$ T cells, respectively. On the other hand, dendritic cells transfected with the mRNA vaccine or its endocytosed immunogens process the MHC class II complex and present it to immune cells. Only antibodies against the S protein are produced via this mechanism, as no other peptides are produced [11–13].

Patients with a history of allergic diseases, especially those experiencing severe reactions, found themselves in a particularly difficult situation. Firstly, there was a lack of available research confirming the long-term safety of COVID-19 vaccines and, secondly, false information about the vaccines was appearing on social media. The aim of the current study was to determine the degree of safety and potential risk of acute allergic reactions after mRNA COVID-19 vaccination among a group of patients predisposed to allergic diseases.

2. Methods

2.1. Data collection

The study was based on survey sampling. The study survey took from May 2021 to February 2022. The study protocol was approved by the Bioethics Committee at the Ludwik Rydygier Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń (KB 344/2021). All participants provided written informed consent to take part in the project.

The study was based on a pre-vaccination questionnaire during patient eligibility assessment for vaccination, and two subsequent questionnaires were completed approximately 21 days after the first and second doses of vaccination. Patients completed the questionnaire on their own, and the data were processed in accordance with the General Data Protection Regulation. The pre-vaccination questionnaire included questions about age, gender and the reason for not being eligible for vaccination at a Vaccination Point. In subsequent questionnaires, participants were asked if any of the following symptoms occurred after vaccination: redness at the injection site, pain at the injection site, pain at the injection site only during pressure, pain in the entire limb, general weakness, headache, temperature >38° Celsius, dizziness, nausea, vomiting, diarrhoea, abdominal pain, chest pain, dyspnoea, muscle pain, hives, itching, conjunctivitis, anaphylactic shock, or other symptoms. Participants were asked to include the time after injection when the symptom(s) occurred and the duration. Due to the nature of the questions asked in the survey and the desire to extend the issues raised, validation of the questionnaire was deemed unnecessary.

2.2. Study participants

Study participants constituted a selected group of 52 patients aged >18 years who, due to a history of severe allergic disease, were not eligible for vaccination at the COVID-19 Vaccination Points available in Poland. Eligibility at the Vaccination Points was conducted by doctors of different specialties, but most frequently not by allergists. The study clinic, one of the few in Europe, made it possible to vaccinate patients in a hospital setting. Initially ineligible patients from different parts of Poland first reported to the Allergology Outpatient Clinic, where an allergy specialist made a decision about the place of vaccination or absolute ineligibility based on the medical history and physical examination. In the case of absence of allergological indications for vaccination in a hospital setting, the doctor issued an appropriate document enabling vaccination at a Vaccination Point. Patients with an increased risk of severe allergic reactions after the injection were referred to vaccinations in a hospital setting. The vaccination was carried out in the Department of Allergology, Clinical Immunology and Internal Diseases, Dr J. Biziel University Hospital No.2 in Bydgoszcz, Poland, in the presence of a physician, in the conditions of intensive allergological care. Emergency equipment was available during the vaccination, and the hospital also had appropriate anaesthetic equipment in the event of an immediate threat to the patient's health or life. All patients were vaccinated with the Pfizer BioNTech Comirnaty preparation, which resulted from the available reserves in the country and the guidelines of the Ministry of Health.

2.3. Statistical analyses

In the descriptive analysis, tables were used in which the number and percentage of responses to individual questions of the questionnaires were presented. Graphical interpretation of these data are shown in vertical bar graphs. The arithmetic mean and standard deviation were also used. The correlation between the two variables was calculated using the Spearman rank correlation coefficient. The nonparametric Mann-Whitney *U* Test was also used to evaluate the differences in one feature between the two populations (groups). All calculations and figures were performed by means of the Statistica 10.0 software and with the Microsoft Excel spreadsheet using standard functions of this program.

3. Results

The study included 52 patients aged >18 years. In total, 76.9% (n = 40) of the participants were women. The average age of participants was 57.3 years; standard deviation accounted for over 30.2% of the mean value, which proves the average age differentiation. Men had a higher average age (64.9 years) than women (55.1 years). The minimum age of participants varied between the sexes and was lower women (24 years); however, the maximum age was similar and highest in women (86 years). Respondents were divided into four age groups according to the results of the median and quartiles. The most numerous group were participants aged 72–86 years (28.8% [n = 15]) and the joint least numerous groups aged 24–42 years and 58–71 years (23.1% [n = 12] each) – see Fig. 1.

In total, 59 responses from 52 participants were given as reasons for vaccination ineligibility in the pre-vaccination questionnaire. The most frequent reasons were anaphylactic shock after drugs administered

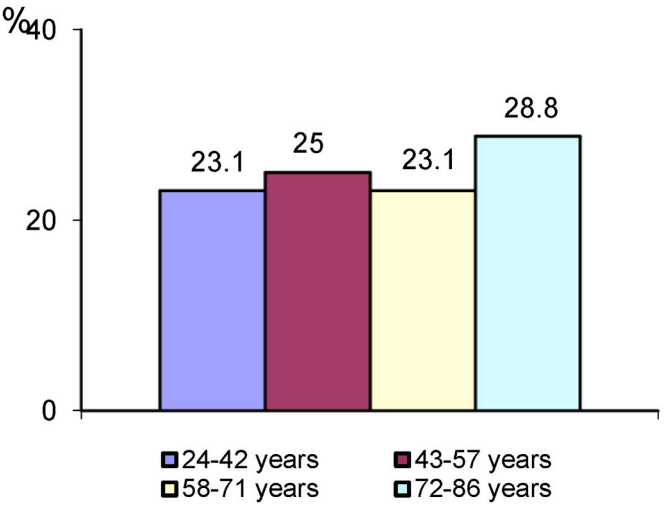

Fig. 1. Distribution of age groups.

parenterally (27.1% [n = 16]) and a past acute allergic reaction, but without the accompanying anaphylactic shock (16.9% [n = 10]). A history of anaphylactic shock after oral drugs was given as the reason for vaccination in a hospital setting (15.3% [n = 9]). All the causes have been collected and summarised in Table 1, and their percentage distribution is shown in Fig. 2.

In the study group, only two participants had been infected with COVID-19 before the vaccination.

Data concerning the frequency of adverse events, the time between vaccination and onset of symptoms, and the duration of symptoms are summarised in Table 2, 3 and 4.

In both vaccinations, an identical percentage of 'other' symptoms was recorded (15.4% [n = 8] each), and the reported ailments included joint pain, a swollen throat, pain in the left eyebrow, difficulty swallowing, hair loss, swollen eyelids, balance disorders and sore throat. In the first vaccination participants did not report problems swallowing, laryngeal oedema, balance disorders or sore throat, and in the second vaccination they experienced no pain in the left eyebrow, difficulty swallowing and eyelid oedema.

The most important differences in the results between the first and second vaccination are presented in Table 5.

In relation to the significance level ($p > 0.05$), there were no statistically significant differences between the first and the second vaccination in terms of symptoms, time and duration of symptoms. No statistically significant differences were found between men and women in the results concerning the symptoms following the first vaccination; however, a statistically significant difference ($p = 0.033$) was observed between men and women regarding the occurrence of redness at the injection site after the second vaccination. A higher rate of redness at the vaccination site was reported in women (32.5% [n = 13]) than in men (8.3% [n = 1]) following the second vaccination. The age of the participants did not correlate statistically with the occurrence of symptoms after the first or second vaccination ($p > 0.05$).

4. Discussion

mRNA vaccines, like any other medical products, may be a potential source of allergens and trigger hypersensitivity reactions, especially in predisposed individuals. Although hypersensitivity to vaccines is relatively rare, a potential occurrence of a severe allergic reaction cannot be ruled out. The anxiety of people with the history of severe allergic reactions or with serious atopic diseases has undoubtedly increased following media coverage of adverse events within 24 h of the first mRNA vaccination, including two reports of anaphylactic reactions within a few minutes of administration of the vaccine. In December 2020 in the US, 21 cases of anaphylaxis were reported after the administration of the first 2 million doses of Pfizer-BioNTech COVID-19 vaccine, while in January 2021, 10 cases of anaphylaxis had been reported after the administration of over 4 million first doses of the Moderna COVID-19 vaccine [14–16].

Most hypersensitivity reactions to vaccines are non-immune in nature, and the mechanism of their development is based primarily on the vaccine toxic reaction, adverse effects or drug interactions [17]. Nevertheless, less frequent, but still clinically important, are hypersensitivity reactions in which the immunological mechanism is based mainly on the formation/presence of sIgE, T-cell response with a shift towards the Th2-dependent response and other responses of the immune system targeting a specific antigen [18]. The most severe and immediately life-threatening anaphylactic reaction classified as type 1 hypersensitivity reaction according to Coombs, occurs as a result of binding of specific antigens to IgE class antibodies and the subsequent degranulation of mast cells, which leads to the development of clinical symptoms. It should be remembered that the development of anaphylaxis may be either immediate or the reaction may be delayed, which translates into the way the patients are treated. Some clinical symptoms connected with vaccination against COVID-19 may occur on the basis of a pseudoallergy, where the previously present sIgM or sIgG, after binding a specific antigen, trigger the classical complement activation pathway, with the release of anaphylatoxins, such as C3a or C5a, responsible for the clinical presentation [19,20]. During the analysis of individual substrates used for the production of an mRNA vaccine, we can observe several potential pathomechanisms.

Table 1
Reasons for vaccination ineligibility.

Reason	n	%
History of anaphylactic shock after drugs administered parenterally	16	27.1
History of anaphylactic shock after drugs administered orally	9	15.3
History of anaphylactic shock after anaesthetic agents	3	5.1
History of anaphylactic shock after food	5	8.5
History of anaphylactic shock after insect sting	6	10.2
Lack of anaphylactic shock but severe allergic reaction	10	16.9
History of angioedema	3	5.1
History of hives	0	0.0
Allergic bronchial asthma	4	6.8
No apparent reason	2	3.4
Another reason	1	1.7
Total	59	100.0

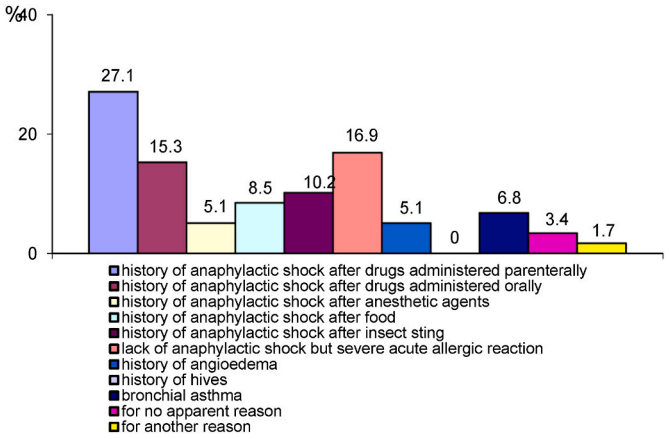

Fig. 2. Distribution of reasons for disqualification.

Table 2
Percentage of individual symptoms after the first and second vaccination.

Symptoms	First vaccination (%)	Second vaccination (%)
Redness at the injection site	26.9	23.1
Pain at the injection site	57.7	59.6
Swelling at the injection site	19.2	9.3
Pain at the injection site only during pressure	21.2	17.3
Pain in the entire limb	17.3	17.3
General weakness	50.0	44.2
Headache	28.8	25.0
Temperature > 38 degrees Celsius	5.8	7.7
Dizziness	13.5	13.5
Nausea	5.8	1.9
Vomiting	1.9	0.0
Diarrhoea	0.0	1.9
Abdominal pain	1.9	3.8
Chest pain	3.8	1.9
Dyspnoea	7.7	5.8
Muscular pain	17.3	25.0
Hives	1.9	0.0
Itching	3.8	1.9
Conjunctivitis	0.0	0.0
Anaphylactic shock	0.0	0.0

Table 3
Percentage of people with selected symptoms, mean time until the occurrence of a symptom and mean duration - first vaccination.

Symptoms	First vaccination (%)	Average time to the occurrence of a symptom (hours)	Average duration of a symptom (hours)
Redness at the injection site	26.9	11.5	108.9
Pain at the injection site	57.7	10.0	58.5
Swelling at the injection site	19.2	10.4	132.0
Pain at the injection site only during pressure	21.2	6.9	26.6
Pain in the entire limb	17.3	9.6	88.0
General weakness	50.0	8.2	49.4
Headache	28.8	7.7	59.4
Temperature > 38 degrees Celsius	5.8	28.0	56.0
Dizziness	13.5	23.4	59.4
Nausea	5.8	6.8	48.7
Vomiting	1.9	24.0	30.0
Diarrhoea	0.0	0.0	0.0
Abdominal pain	1.9	14.0	5.0
Chest pain	3.8	5.3	4.3
Dyspnoea	7.7	4.8	8.2
Muscular pain	17.3	11.0	56.6
Hives	1.9	24.0	72.0
Itching	3.8	48.0	60.0
Conjunctivitis	0.0	0.0	0.0
Anaphylactic shock	0.0	0.0	0.0

Table 4
Percentage of people with selected symptoms, mean time until the occurrence of a symptom and mean duration - second vaccination.

Symptoms	Second vaccination (%)	Average time to the occurrence of a symptom (hours)	Average duration of a symptom (hours)
Redness at the injection site	23.1	9.6	67.7
Pain at the injection site	59.6	13.4	49.2
Swelling at the injection site	9.3	10.2	139.2
Pain at the injection site only during pressure	17.3	5.0	26.3
Pain in the entire limb	17.3	9.0	81.3
General weakness	44.2	14.2	50.9
Headache	25.0	13.2	48.6
Temperature >38° Celsius	7.7	29.3	60.8
Dizziness	13.5	25.4	64.3
Nausea	1.9	1.0	1.0
Vomiting	0.0	0.0	0.0
Diarrhoea	1.9	12.0	24.0
Abdominal pain	3.8	81.0	36.0
Chest pain	1.9	1.0	48.0
Dyspnoea	5.8	8.6	64.0
Muscular pain	25.0	14.2	45.4
Hives	0.0	0.0	0.0
Itching	1.9	10.0	48.0
Conjunctivitis	0.0	0.0	0.0
Anaphylactic shock	0.0	0.0	0.0

4.1. Pegylated lipid nanoparticles

The first drug administered in pegylated form was doxorubicin, and the aim of such an action was to increase the hydrophilicity of the liposomal drug carriers, which significantly improved the stability of the molecule and clearly slowed the rate of drug removal through the reticuloendothelial system. Unfortunately, severe hypersensitivity reactions were reported only a year after the drug was introduced. Later studies showed that in patients who developed severe clinical symptoms (mainly severe hypotension), IgM or IgG antibodies against PEG (polyethylene glycol) were present in the serum, which activated complement in the classical pathway. It, in turn, was confirmed by measuring the intravascular production of sC5b-9 complement cleavage products in the serum of patients 10 min after the injection of the drug. C5a activated mast cells, through the degranulation of effector substances, led to the development of clinical symptoms. This mechanism is currently being 'cheated' by initial administration of pegylated lipid nanoparticles without doxorubicin, which show much lower reactivity, accelerate the removal of sIgM and sIgG from the serum and significantly reduce the risk of developing a severe allergic reaction after administration of molecules containing drugs [21–24]. Pegylated lipid nanoparticles are an extremely important component of an mRNA vaccine, ensuring its stability and facilitating reaching the target site. However, there are currently no studies available to evaluate the role of pegylated lipid molecules of the mRNA vaccine in the development of acute allergic reactions following vaccinations. Nevertheless, the occurrence of anaphylaxis after the administration of the first dose of the vaccine may lead to the suggestion that polyethylene glycol is the main factor contributing to the pathomechanism of the development of clinical symptoms. Moreover, it is currently the only excipient in the introduced mRNA vaccines with recognised allergenic potential. The severity and rapid onset of the reported vaccine reactions additionally increase the suspicion towards PEG [14,25].

4.2. Nucleic acid (mRNA)

Theoretically, mRNA itself could also contribute to the development of symptoms. The interaction of PAMP (pathogen-associated molecular patterns), which also include viral single-strand mRNA, with pattern recognition receptors may activate the immune system 'nonspecifically'. In addition, activation of the intrinsic pathway of the coagulation cascade directly by mRNA leading to the production of bradykinin is also possible, which may contribute to the development of symptoms of angioedema and anaphylactoid reaction. However, for this to take place, it would be necessary to damage the lipid molecule that protects the mRNA of the vaccine and to release nucleic acid into the extracellular environment, which is extremely unlikely [14,26,27].

Regardless of the pathomechanism, severe allergic reactions after COVID-19 vaccination constitute an important element limiting the safety of mRNA vaccines. In the current study, there was not a single anaphylactic reaction, which is certainly due to the limited number of patients in the study group. The results are consistent with those presented in the world reports, where anaphylaxis occurred on average 11 times per million vaccinations (concerning Pfizer Bio-Ntech COVID-19) [28]. It should also be mentioned that, despite the existing predisposition to allergic diseases, the most common symptoms in the study participants were local post-vaccination reactions (i.e. pain and redness at the injection site, and mild general symptoms in the form of general weakness and headache). These symptoms do not pose a great threat to the patient and only lead to temporary discomfort. The symptoms are likely to be related to the correct immune response of the body to the administration of a foreign antigen and indirectly indicate that the 'desired' reaction of the immune system has been obtained.

4.3. Limitations

The study has several limitations, including the sampling technique, the sample source and sample size; however, these factors were conditioned by external factors and are beyond the control of the study investigators.

Table 5
Differences in the results between the first and second vaccination.

symptom	Rank sum first	Rank sum second	U	Z	p-value	Z adjusted	p-value	Valid N first	Valid N second	2*1sided exact p
Redness at the injection site	2782.0	2678.0	1300.0	0.335	0.738	0.446	0.655	52	52	0.739
How long after the vaccination did the symptoms occur?	193.5	157.5	79.5	0.206	0.837	0.209	0.835	14	12	0.820
How long did the symptoms last?	214.5	136.5	58.5	1.286	0.198	1.329	0.184	14	12	0.193
Pain at the injection side	2704.0	2756.0	1326.0	−0.166	0.868	−0.194	0.846	52	52	0.869
How long after the vaccination did the symptoms occur?	976.0	915.0	419.0	0.656	0.512	0.663	0.507	30	31	0.514
How long did the symptoms last?	955.0	936.0	440.0	0.353	0.724	0.365	0.715	30	31	0.726
Swelling at the injection site	2860.0	2600.0	1222.0	0.842	0.400	1.383	0.167	52	52	0.401
How long after the vaccination did the symptoms occur?	78.0	42.0	23.0	−0.184	0.854	−0.187	0.852	10	5	0.859
How long did the symptoms last?	78.5	41.5	23.5	−0.122	0.903	−0.130	0.897	10	5	0.859
Pain at the injection site only during pressure	2782.0	2678.0	1300.0	0.335	0.738	0.490	0.624	52	52	0.739
How long after the vaccination did the symptoms occur?	123.0	87.0	42.0	0.532	0.595	0.537	0.591	11	9	0.603
How long did the symptoms last?	118.5	91.5	46.5	0.190	0.849	0.204	0.839	11	9	0.824
Pain In the entire limb	2656.5	2699.5	1321.5	0.026	0.979	0.040	0.968	51	52	0.976
How long after the vaccination did the symptoms occur?	87.5	83.5	38.5	0.132	0.895	0.134	0.894	9	9	0.863
How long did the symptoms last?	84.5	86.5	39.5	−0.044	0.965	−0.045	0.964	9	9	0.931
General weakness	2808.0	2652.0	1274.0	0.504	0.614	0.583	0.560	52	52	0.616
How long after the vaccination did the symptoms occur?	567.5	657.5	216.5	−1.643	0.100	−1.654	0.098	26	23	0.099
How long did the symptoms last?	633.5	591.5	282.5	−0.321	0.749	−0.324	0.746	26	23	0.743
Headache	2782.0	2678.0	1300.0	0.335	0.738	0.436	0.663	52	52	0.739
How long after the vaccination did the symptoms occur?	180.0	226.0	60.0	−1.704	0.088	−1.716	0.086	15	13	0.088
How long did the symptoms last?	217.0	189.0	97.0	0.000	1.000	0.000	1.000	15	13	1.000
Temperature >38° Celsius	2704.0	2756.0	1326.0	−0.166	0.868	−0.382	0.702	52	52	0.869
How long after the vaccination did the symptoms occur?	–	–	–	–	–	–	NS	–	–	–
How long did the symptoms last?	–	–	–	–	–	–	NS	–	–	–
Dizziness	2730.0	2730.0	1352.0	−0.003	0.997	−0.005	0.996	52	52	1.000
How long after the vaccination did the symptoms occur?	51.0	54.0	23.0	−0.128	0.898	−0.129	0.898	7	7	0.902
How long did the symptoms last?	49.5	55.5	21.5	−0.319	0.749	−0.324	0.746	7	7	0.710
Nausea	2782.0	2678.0	1300.0	0.335	0.738	1.005	0.315	52	52	0.739
How long after the vaccination did the symptoms occur?	–	–	–	–	–	–	NS	–	–	–
How long did the symptoms last?	–	–	–	–	–	–	NS	–	–	–
Vomiting	2782.0	2678.0	1300.0	0.335	0.738	1.407	0.159	52	52	0.739
How long after the vaccination did the symptoms occur?	–	–	–	–	–	–	NS	–	–	–
How long did the symptoms last?	–	–	–	–	–	–	NS	–	–	–
Diarrhoea	2704.0	2756.0	1326.0	−0.166	0.868	−0.981	0.327	52	52	0.869
How long after the vaccination did the symptoms occur?	–	–	–	–	–	–	NS	–	–	–
How long did the symptoms last?	–	–	–	–	–	–	NS	–	–	–
Abdominal pain	2704.0	2756.0	1326.0	−0.166	0.868	−0.572	0.567	52	52	0.869
How long after the vaccination did the symptoms occur?	–	–	–	–	–	–	NS	–	–	–
How long did the symptoms last?	–	–	–	–	–	–	NS	–	–	–
Chest pain	2756.0	2704.0	1326.0	0.166	0.868	0.572	0.567	52	52	0.869
How long after the vaccination did the symptoms occur?	–	–	–	–	–	–	NS	–	–	–
How long did the symptoms last?	–	–	–	–	–	–	NS	–	–	–
Dyspnoea	2756.0	2704.0	1326.0	0.166	0.868	0.382	0.702	52	52	0.869
How long after the vaccination did the symptoms occur?	–	–	–	–	–	–	NS	–	–	–
How long did the symptoms last?	–	–	–	–	–	–	NS	–	–	–
Muscle pain	2626.0	2834.0	1248.0	−0.673	0.501	−0.951	0.342	52	52	0.503
How long after the vaccination did the symptoms occur?	91.0	162.0	46.0	−0.801	0.423	−0.823	0.411	9	13	0.431
How long did the symptoms last?	115.5	137.5	46.5	0.768	0.443	0.790	0.429	9	13	0.431
Hives	2756.0	2704.0	1326.0	0.166	0.868	0.981	0.327	52	52	0.869
How long after the vaccination did the symptoms occur?	–	–	–	–	–	–	NS	–	–	–
How long did the symptoms last?	–	–	–	–	–	–	NS	–	–	–
Itchiness	2756.0	2704.0	1326.0	0.166	0.868	0.572	0.567	52	52	0.869
How long after the vaccination did the symptoms occur?	–	–	–	–	–	–	NS	–	–	–
How long did the symptoms last?	–	–	–	–	–	–	NS	–	–	–

(*continued on next page*)

Table 5 (*continued*)

symptom	Rank sum first	Rank sum second	U	Z	p-value	Z adjusted	p-value	Valid N first	Valid N second	2*1sided exact p
Conjunctivitis	2730.0	2730.0	1352.0	−0.003	0,.997	–	–	52	52	–
How long after the vaccination did the symptoms occur?	–	–	–	–	–	–	NS	–	–	–
How long did the symptoms last?	–	–	–	–	–	–	NS	–	–	–
Anaphylactic shock	2730.0	2730.0	1352.0	−0.003	0.997	–	–	52	52	–
How long after the vaccination did the symptoms occur?	–	–	–	–	–	–	NS	–	–	–
How long did the symptoms last?	–	–	–	–	–	–	NS	–	–	–
Others	2723.5	2736.5	1345.5	−0.039	0.969	−0.062	0.950	52	52	0.966
How long after the vaccination did the symptoms occur?	68.5	67.5	31.5	0.000	1.000	0.000	1.000	8	8	0.959
How long did the symptoms last?	71.0	65.0	29.0	0.263	0.793	0.263	0.792	8	8	0.798

5. Conclusions

In light of limited COVID-19 treatment and the high mortality rate, vaccination should be recommended, including for those people predisposed to allergic diseases. Based on the study results, it can be concluded that mRNA COVID-19 vaccines show a favourable safety profile for patients with a history of allergic disease and constitute the optimal strategy for fighting the SARS-CoV-2 pandemic. The correct assessment of patient eligibility for vaccination and individualisation of prophylaxis based on the latest clinical and scientific reports are of great importance. Results from this study support the recommendation that individuals who are particularly at risk of developing acute allergic reactions after vaccinations should be vaccinated with the assistance of a physician and with emergency equipment available. Providing this environment for vaccination will prevent any possible complications and help alleviate the anxiety in those people who have been reluctant to receive the COVID-19 vaccine due to the fear of allergic complications [29,30].

Ethical approval

The study protocol was approved by the Bioethics Committee at the Ludwik Rydygier Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń (KB 344/2021).

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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