Observational Study

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Suspected adverse events following immunization against SARS-CoV2 in a university hospital in 2021

Observational study

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Abstract

Aim: Vaccination against SARS-CoV2 has been proposed as a fundamental element for the control of the pandemic. This study aimed to describe the suspected adverse reactions (ADR) reported by vaccinated hospital workers.

Methods: A descriptive study of suspected ADR was conducted between January and March 2021. The suspected ADR were identified using a specifically designed electronic form and spontaneous reporting. Data were also collected regarding the characteristics of the professionals, vaccine administered, severity, and outcome of ADR.

Results: 8169 professionals received 2 doses of SARS-CoV2 vaccine (6672 Comirnaty® and 1497 Spikevax®) and 894 reports of suspected ADR were reported (762 for Comirnaty® and 132 for Spikevax®), resulting in a cumulative ADR incidence of 10.94% (95%CI: 10.27-11.62). The majority of ADR were reported only after the second dose, 497 (56.2%), while 211 (23.6%) were reported only after the first dose and 186 (21%) after both doses. The symptoms were mostly mild, did not require medical assistance, and disappeared within approximately 3 days. One hundred and seventeen professionals had a history of COVID-19 infection. These studies reported, statistically significant, more suspected ADR after the first dose (42.7%) than those with no history of COVID-19 (20.7%). Among professionals, more ADR occurred after the first dose with the Spikevax® vaccine (41.6%) than with the Comirnaty® vaccine (20.5%).

Conclusion: The majority of suspected ADR reported were described in the summary of product characteristics (SmPC). Professionals with a history of COVID-19 reported more suspected ADR after the first dose than did those without a history.

Abbreviations: ADR = adverse drug reaction, HUB = Bellvitge University Hospital, IQR = interquartile range, PhFV = pharmacovigilance program, SEFV = Spanish pharmacovigilance system, SmPC = summary of product characteristics.

Keywords: COVID-19, COVID-19 vaccine, pharmacovigilance, SARS-CoV-2, SARS-CoV-2 vaccine, viral vaccines

1. Introduction

Despite improvements in treatment for COVID-19 over the months, no curative treatment has been available to date. Therefore, vaccination has played a key role in controlling the pandemic.[1]

Vaccination campaigns began in Catalonia in December 2020, following the indications of the vaccination strategy defined in the document: *COVID-19 Vaccination strategy in Spain*. Priority was given to populations considered essential, including healthcare/nursing home personnel, residents, and dependent elderly individuals. The strategy was updated according to the epidemiological situation, availability of vaccines, and emergence of new information.[2]

Authorization for COVID-19 vaccines was granted as a result of the clinical trials that emerged. The European Medicines Agency first authorized the Comirnaty® vaccine developed by BioNTech/Pfizer[3] on December 21st, 2020, Spikevax® developed by Moderna/Lonza[4] on January 6th, 2021, the Vaxzevria® vaccine of AstraZeneca[5] on January 29th, 2021, and the Janssen® COVID-19 vaccine[6] on March 15th, 2021. All patients received conditional authorization and underwent additional follow-up with intensive monitoring.

The authors have no funding and conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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The available information on the safety of the vaccines in humans was evaluated by regulatory agencies, which permitted the authorization of these vaccines for presenting a favorable risk/benefit ratio. Adverse effects described as frequent in the summary of product characteristics (SmPC) were pain at the injection site, fatigue or feeling tired, headache, myalgia, chills, arthralgia, fever, and lymphadenopathies. However, there is a need for additional information on vaccine use in the general population, outside the context of clinical trials.[7] An analysis has been published on the reports received by the Vaccine Adverse Event Reporting System, a United States of America vaccine safety surveillance program run by the Centers for Disease Control and Prevention and the Food and Drug Administration, regarding COVID-19 mRNA vaccines. This report analyzed 3908 adverse reactions gathered during December 2020 in a population with an average age of 42 years, of which 80% were women and 95% were referred to the vaccine developed by BioNTech/Pfizer. The most frequently described adverse reactions are fatigue, pain, chills, headache, dizziness, and paresthesia.[8]

Europe has established a pharmacovigilance plan network with different strategies to evaluate the safety of post-market COVID-19 vaccines, which includes encouraging the spontaneous reporting of suspected adverse reactions to vaccines through the options offered by the Spanish Pharmacovigilance System (SEFV).[7] The main objective of the pharmacovigilance plan is to identify adverse events that may not have been detected in clinical trials.[9,10] On the other hand, the regulatory agencies provide updated and aggregated information regarding the suspected adverse drug reaction (ADR) reports received. The Spanish Agency of Medicines and Health Products provides regular information on pharmacovigilance reports on the COVID-19 vaccine.[11]

The pharmacovigilance program (PhFV) carried out by the Clinical Pharmacology Department of Bellvitge University Hospital (HUB) in collaboration with other departments of the hospital has intensified efforts aimed at identifying the appearance of these suspected ADR among professionals who received the vaccine at HUB, along with facilitating the delivery of these reports to the SEFV. This study aimed to describe suspected ADR collected from vaccinated hospital workers between January and March 2021.

2. Methodology

2.1. Study design and population

This was an observational, retrospective, and descriptive study of suspected ADR identified among healthcare and non-healthcare professionals included in the HUB vaccination campaign from January 5 to March 31, 2021.

2.2. Inclusion and exclusion criteria

Included were healthcare and non-healthcare professionals from the HUB and from external collaborating companies such as the blood bank, logistics services, emergency medical services, ambulances, and others who received 1 of the COVID-19 vaccines at the hospital and reported a suspected ADR to the PhFV of the HUB during the study period, either after the first and/or second dose between January and March 2021.

2.3. Vaccine administration strategy and PhFV

On January 5th, 2021, vaccines were administered to healthcare and non-healthcare professionals in the HUB. The first dose administered corresponded to the first vaccine available, which was Comirnaty® of BioNTech/Pfizer; as of February, Spikevax® of Moderna/Lonza was also administered jointly, according to the availability of the vaccines.

The vaccination strategy criteria followed the guidelines defined by the Spanish National Health System and included in the COVID-19 vaccination strategy document. This study underwent several modifications, 5 of which appeared during the study period. One of the relevant changes in version 4 of the aforementioned document dated February 26th[2] was to administer a single dose of the vaccine to those under the age of 55 with a history of COVID-19.

HUB is a 770-bed tertiary care public hospital for adults in Barcelona (Catalonia, Spain). Since 2007, HUB has a PhFV that, among other activities, carries out intensive monitoring of suspected ADR as the cause of emergency department patients to be admitted for in-hospital care and also collects the suspected ADR reports from HUB professionals. This program facilitates the reporting of ADR to the SEFV.[12] With the rollout of COVID-19 vaccination, HUB's PhFV has redirected its activities, on the one hand, to closely monitor the safety issues regarding the vaccination of hospital workers and, on the other hand, to identify possible unknown ADR. To this end, efforts have been intensified to encourage spontaneous reporting among vaccination professionals. Emails, including the email address and telephone number of the Clinical Pharmacology Department, were sent to all professionals. An online ADR report form was created with access to the personnel cited for vaccination so that they could file a report if they deemed it necessary, which was specifically designed to facilitate the identification of signals regarding vaccine toxicity. This form includes a list of ADR described in the SmPC and an open section for other undescribed ADR.

2.4. Selection process

The sources of identification of the suspected ADR were:

1. An electronic ADR report form, specifically designed to which the staff member summoned for vaccination, had access to file a report that could be related to the administration of the vaccine. A list of known ADR (pain at the injection site, fatigue, headache, myalgia, arthralgia, chills, fever, lymphadenopathies, urticarial rash, and digestive symptoms) and a free-report section.
2. Spontaneous report to the Clinical Pharmacology Department staff through other means (telephone, email, in-person) already provided by HUB's PhFV.

2.5. Study variables

Data were collected on the characteristics of the professionals, including demographic data, pathological history, and history of COVID-19. The descriptor terms of the suspected ADR were collected from the data on suspected ADR. The date of ADR onset, number of general symptoms, ADR duration, severity, outcome, and causality algorithm were also recorded. The data gathered regarding the vaccine included name, site (arm) of administration, batch number, and date of vaccination.

The definition of ADR employed was established in Royal Decree 577/2013, which regulates pharmacovigilance in Spain.[13] The Medical Dictionary for Regulatory Activities version 24.0 was used for the coding and classification of the descriptor terms for reactions. The imputation methods of the SEFV were followed to construct the causality algorithm.[14]

2.6. Follow-up

The professionals were followed up via electronic medical records to determine if they had required medical assistance to treat the symptoms and to assess severity and outcome. In cases of doubt or lack of information in the electronic medical records, the information was collected via a phone call to the professional in itself.

2.7. Statistical analysis

A descriptive analysis of the variables was performed. Results were expressed as absolute and relative frequencies for qualitative variables and as means, standard deviations, or medians and interquartile ranges (IQR) when appropriate for quantitative variables. A chi-square test was performed for the comparison of percentages and Student *t* test for the comparison of means if a normal distribution appeared. Statistical significance was determined at a *P* value of <.05, with a 95% confidence interval. Statistical analysis was performed using Microsoft Office Excel 2007 and Statistical Package of Social Sciences version 25.

No calculation of the sample size was performed because all suspected ADR reported by professionals who met the inclusion criteria during the study period were collected.

2.8. Ethical aspects

The HUB Drug Research Ethics Committee approved the study protocol. All suspected ADR of special interest were reported to the Catalan Pharmacovigilance Center of the SEFV.[15]

The retrospective design of the study allows us to consider that it is not necessary to obtain the informed consent of the included patients. The treatment of the information met the same quality standards in terms of data protection. The database is part of the hospital's information systems and has the same confidentiality protection guarantees as the rest of the HUB's computerized clinical history.

3. Results

From January 5th and March 31st, 2021, 9549 first doses of the vaccine were administered (6906 of Comirnaty® and 2643 of Spikevax®) and 8169 s doses (6672 of Comirnaty® and 1497 of Spikevax®). Among those vaccinated during the same period, 894 professionals reported suspected vaccine-associated ADR. Only 1 dose was administered in 9 cases as they had the disease, and according to the state recommendations of February 26, 2021, a second dose was not necessary if the professional was under 55 years of age. Of the 894 patients, 211 (23.6%) reported a suspected ADR after the first dose. Of the 885 patients receiving the 2 doses, 497 (56.2%) presented a suspected ADR with only the second dose, and 186 (21%) with both doses. Among the 8169 professionals who received the 2 doses of vaccine (full vaccination), the percentage of cases that reported a suspected ADR to the vaccine in 1 of the 2 doses (894 cases) was 11%.

3.1. Baseline characteristics

The mean age of the population reporting a suspected ADR was 39 years (range, 18–69 years), and 696 (78%) were women. Regarding the professional category, 317 (35.5%) were nursing professionals, 294 (33%) corresponded to other healthcare professionals (nursing assistants, laboratory, and radiology technicians), 146 (16.3%) were non-healthcare professionals, and 137 (15.3%) were physicians. There was a history of chronic disease in 148 (16.6%) cases, where hypertension was present in 26 cases (3%) and thyroid alterations were present in 24 cases (2.7%).

A history of COVID-19, confirmed by a positive diagnostic test in the clinical history, was present in 117 cases (13%).

3.2. Description of suspected adverse reactions

Table 1 presents the most common adverse effects, differentiated according to whether they appeared in the first or second dose.

Among the other suspected ADR (Table 1), episodes of herpes simplex (6 cases) and herpes zoster (5 cases) were reported after the first dose, as well as an episode of thrombophlebitis of the thoracoepigastric vein after the first dose and another episode of phlebitis at the same location after the second dose. These 2 venous episodes were related to the Comirnaty® vaccine and the patient recovered favorably.

Table 1

Most common adverse reactions after the 1st and 2nd doses.

	1st dose (n = 894)	2nd dose (n = 885)
Pain at injection site	297 (33.2%)	550 (62.1%)
Fatigue	143 (16%)	479 (54.1%)
Headache	129 (14.4%)	391 (44.2%)
Myalgia	93 (10.4%)	422 (47.7%)
Arthralgia	54 (6%)	287 (32.4%)
Chills	69 (7.7%)	327 (36.9%)
Fever	64 (7.2%)	271 (30.6%)
Gastrointestinal disorders	52 (5.8%)	159 (18%)
Lymphadenopathies	38 (4.3%)	61 (6.9%)
Urticarial rash	3 (0.3%)	1 (0.1%)
Other	61 (6.8%)*	65 (7.3%)**

*10 cases of dizziness, 6 of herpes simplex, 6 of paresthesia, 5 of herpes zoster, 4 of delayed local reaction, 3 of oral canker sores, 3 of non-urticarial skin rashes, and 3 episodes of coughing
**9 cases of dizziness, 6 of non-urticarial rash, 4 of insomnia, 3 of oral canker sores, 3 of abdominal pain and 3 of nonspecific chest pain.

The median duration of symptoms was 2 days (IQR 1-3 days) for the first dose, with a mean of 3,7 days and a range of 1 to 36 days. The median duration of symptoms at the second dose was 2 days (IQR 1-2 days), with a mean of 2,8 days and a range of 1 to 60 days.

A specific analysis was performed for the 6 most common general symptoms (fatigue, headache, myalgia, arthralgia, chills, and fever). After the first dose, 225 (25.2%) professionals reported one of these general symptoms and 619 (70%) reported them after the second dose. Since some professionals reported the occurrence of several of these symptoms simultaneously, Figure 1 shows the distribution of professionals by the number of general symptoms reported simultaneously according to whether they were reported after the first or second dose.

3.3. Healthcare demand, outcome, severity, and causality of suspected ADR

Among the 397 professionals who presented with suspected ADR after the first dose, 36 (9%) required medical assistance (20 consulted in a primary care center and 16 in the hospital's emergency room), and 373 cases (94%) had recovered at the time of termination of the study. Only 1 case was considered serious with thrombophlebitis of the thoracoepigastric vein. In 369 (93%) cases, the association between the vaccine and ADR was considered probable, in 25 (6.3%) cases possible, in 2 cases defined, and in 1 case conditional.

Among the 683 professionals who presented with a suspected ADR after the second dose, 57 (8.3%) requested medical assistance (1 case required hospital admission for pneumonia, 41 consulted in a primary care center, and 15 in the hospital's emergency room). Six hundred and fifty-five patients (97.3%) had recovered at the time of terminating the study, and 2 cases were considered severe (pneumonia and phlebitis of the thoracoepigastric vein in a patient different from the 1 presented with the first dose). In 664 (97.2%) cases, the association between the vaccine and ADR was considered probable, in 17 (2.5%) cases, and in 2 cases definite.

3.4. Professionals with a history of COVID-19

Among the professionals who reported a suspected vaccine-associated ADR, 117 (13%) had a history of SARS-CorV-2 infection.

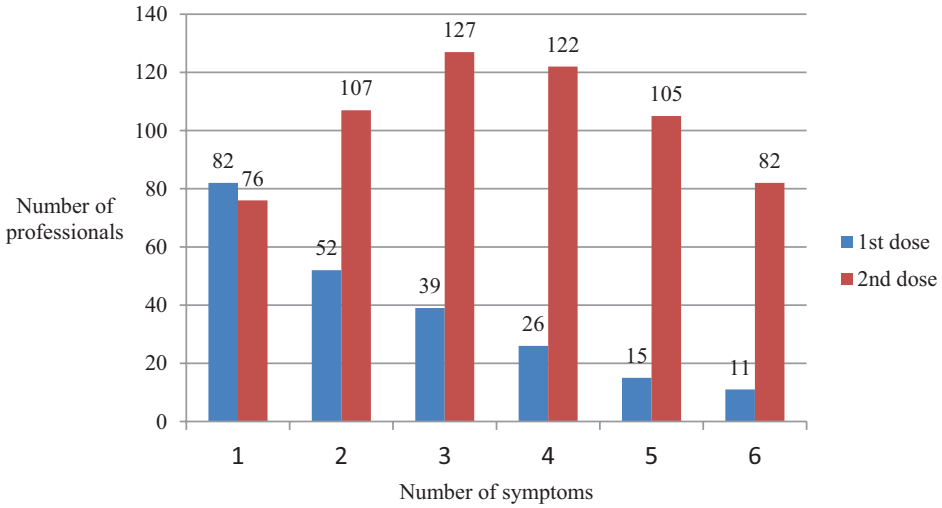

Figure 1. Distribution of professionals by number of general symptoms presented according to whether reported after the 1st or 2nd dose.

The mean age was 39 years, similar to that of the whole study group, regardless of SARS-CorV-2 infection. There was a higher percentage of men with a history of COVID-19 than without, 39 (33.3%) versus 159 (20.5%). This difference was statistically significant (P = .002). Only 7 (6%) patients were admitted to the hospital for COVID-19, 2 of whom were in intensive care. The mean time from COVID-19 diagnosis (positive PCR) to vaccine administration was 6.74 months, with a median of 8. In 45 (38.5%) cases, the vaccine was administered less than 6 months after contracting the disease and after less than 3 months in 25 (21.4%) cases (see Fig. 2).

Among professionals with a history of COVID-19, the Comirnaty® vaccine was employed in 88 (75.2%) cases and Spikevax® vaccine in 29 (24.8%). Among professionals without a history of COVID-19, 674 (86.7%) received the Comirnaty® vaccine and 103 (13.3%) received Spikevax®. The proportion of patients who received the Moderna vaccine was higher than that of Pfizer/Biontech among those who had contracted COVID-19; this difference was statistically significant (P = .001).

Table 2 shows the number of reports received according to the dose in the 2 groups (with or without a history of COVID-19). More ADR were reported after the first dose than after the second dose by professionals who had SARS-Cov2 infection when compared to those who had not had the disease (P < .05). Figure 3 shows the suspected ADR reported according to whether they appeared after the first or second dose.

With respect to the number of general symptoms (fatigue, headache, myalgia, arthralgia, chills and fever), the mean was 1.73 symptoms for professionals with a history of COVID-19 after the first dose and 0.45 for those without (P-value <.001; 95%CI: [-0.5,-1.01]); while the mean of general symptoms for professionals with a history of COVID-19 after the second dose was 2.11 and 2.51 for those without (P value: .137; 95%CI: [-0.2, +0.8]). Figure 4 shows the distribution of the number of general symptoms per group.

The mean duration of symptoms was 3.24 days for the first dose among professionals with a history of COVID-19, and 3.79 for those without (P value: .068; 95%CI: [-0.8, +1.9]). As for the second dose, the mean duration was 2.09 for professionals with a history of COVID-19 and 2.91 for those without (P value: .024; 95%CI: [-0.4, +2]).

Regarding the demand for care, outcome, severity, and causality criteria of suspected ADR, there were no differences between the 2 groups, either with the first or second dose.

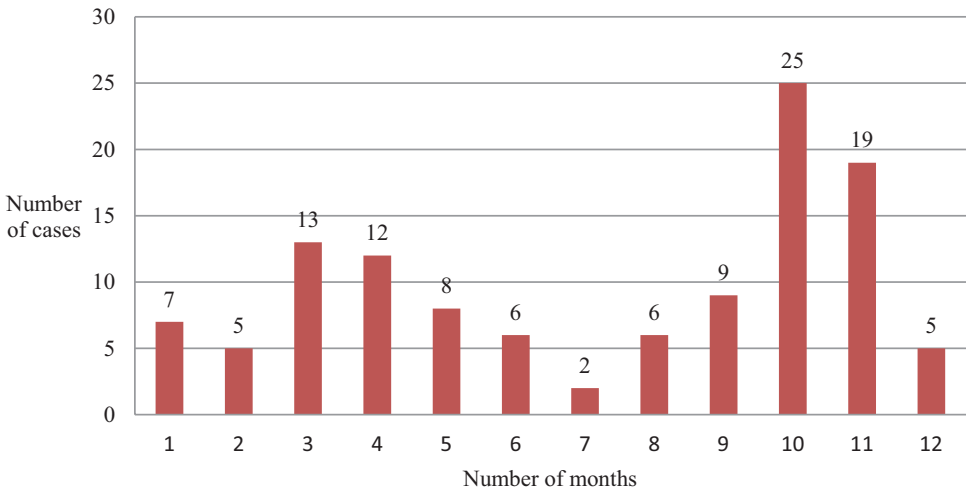

Figure 2. Months from diagnosis of COVID-19 to first dose of vaccine.

Table 2

Number of ADR according to dose and history of COVID-19.

	History of covid		No history of covid	
Number ADR 1st dose	50	42.7%	161	20.7%
Number ADR 2nd dose	41	38%*	456	58.7%
number ADR 1st and 2nd dose	26	24%*	160	20.6%

*Calculated on 108 cases where the 2 doses of vaccine were administered.
ADR = adverse drug reaction.

3.5. Professionals vaccinated with Comirnaty® or Spikevax®

Among professionals who reported a suspected vaccine-associated ADR, 762 (85.2%) had received the Comirnaty® vaccine and 132 (14.8%) received the Spikevax® vaccine.

With respect to the 6672 professionals who received the 2 doses of the Comirnaty® vaccine (full vaccination), the percentage of cases that reported a suspected vaccine-associated ADR with 1 of the 2 doses was 11.42% (95% CI:10.72-12.13; 762 cases). Among the 1497 professionals who received the 2 doses of the Spikevax® vaccine (full vaccination), 8.82% (95% CI:7.38-10.25; 132 cases) reported suspected vaccine-associated ADR with 1 of the 2 doses, which was statistically lower than that with comirnaty exposure.

The mean age was 38 years for those receiving Comirnaty® and 42.5 years-old for those receiving Spikevax® (p 0.58; CI[-4.9, -0.6]). The sex distribution was similar between the 2 vaccine groups, with 594 (78%) women receiving Comirnaty® and 102 (77.3%) receiving Spikevax®.

Among the patients who received Comirnaty®, 88 (11.5%) had COVID-19 compared with 29 (22%) who received Spikevax®. This difference was statistically significant (P = .001).

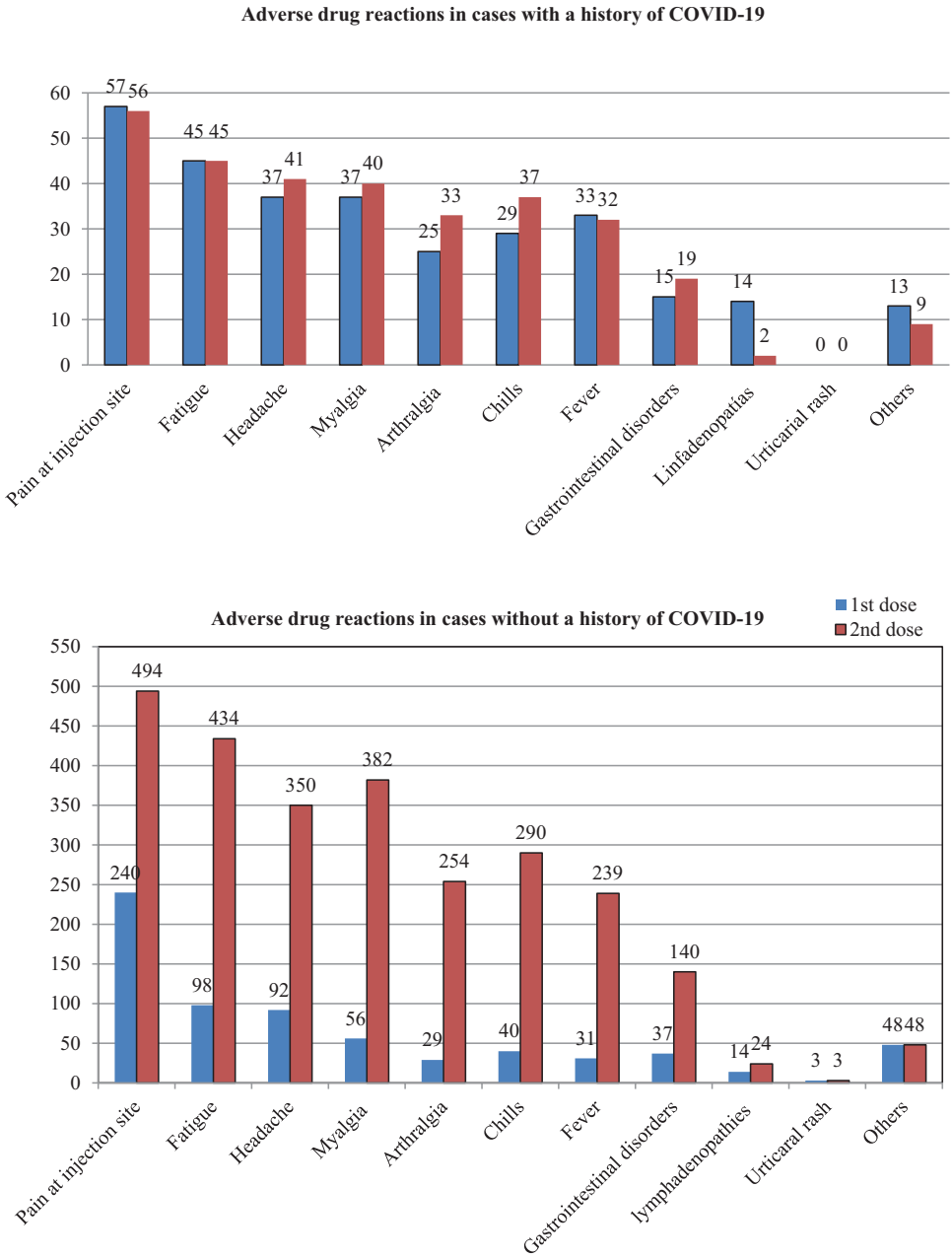

Figure 3. Most common adverse reactions after the 1st and 2nd doses in professionals with or without a history of COVID-19.

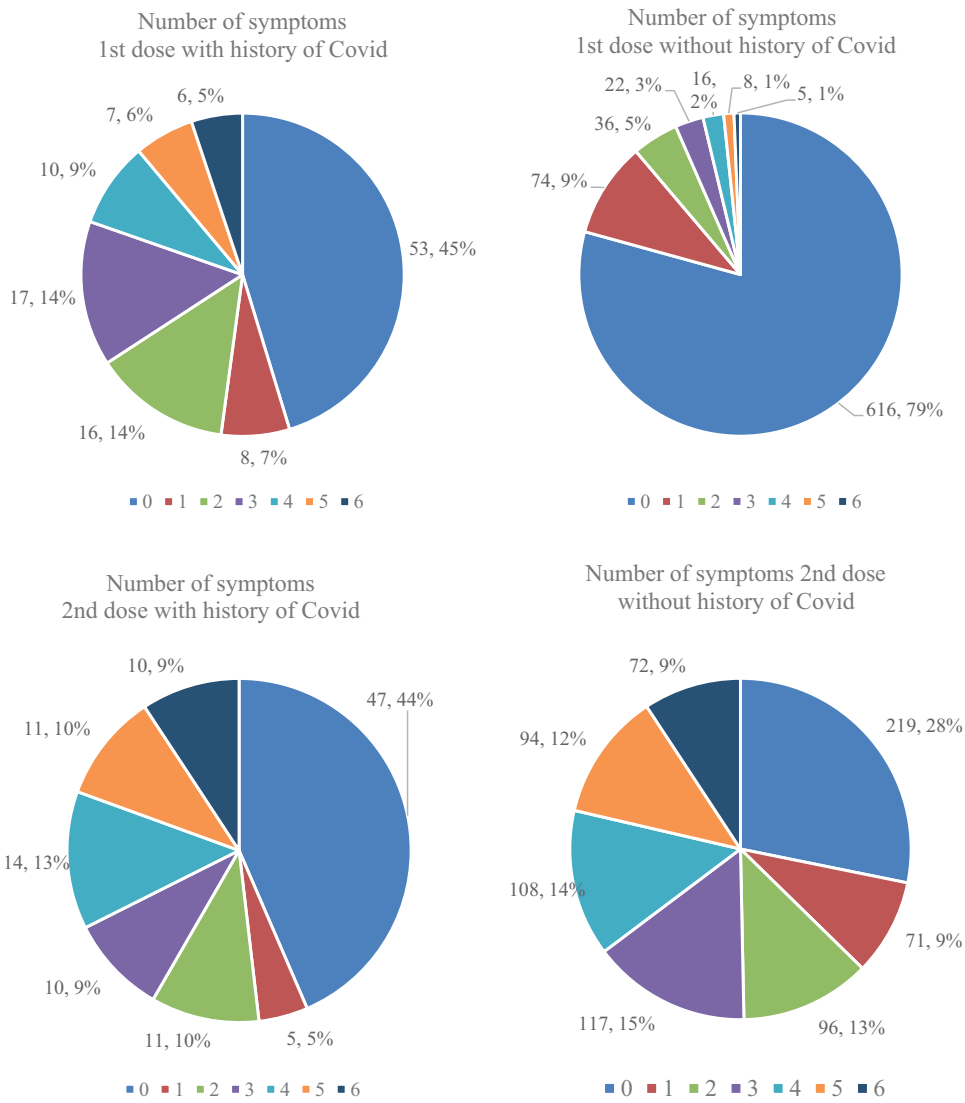

Figure 4. Number of symptoms depending on whether they have a history of COVID-19 or not.

Of the 762 patients vaccinated with Comirnaty®, 301 (39.5%) reported a suspected ADR after the first dose. One patient did not receive the second dose as they had disease and were under 55 years of age. Of the 761 patients who received the second dose, 606 (79.6%) had suspected ADR after the second dose. Of the 132 patients vaccinated with Spikevax®, 96 (73%) reported a suspected adverse reaction after the first dose. In 8 cases, the second dose was not administered, as they had had the disease and were under 55 years of age. Of the 124 patients who received the second dose, 77 (62%) had suspected ADR after the second dose. Table 3 describes the number of reports received according to the dose in the 2 groups. Professionals who received Spikevax® reported more ADR after the first dose than after the second dose.

Figure 5 shows the suspected ADR reported based on whether they appeared after the first or second dose.

With respect to the number of general symptoms (fatigue, headache, myalgia, arthralgia, chills, and fever), the mean symptoms were 0.49 for professionals receiving the first dose of Comirnaty® and 1.32 for Spikevax® (*P* value <.001; 95%CI: [-1.06,-0.6]), while the mean symptoms for professionals receiving the second dose were 2.5 for Comirnaty® and 2.2 for Spikevax® (*P* = .09; 95%CI: [-0.96, +0.8]). Figure 6 shows the distribution according to the number of general symptoms per group.

The mean duration of symptoms was 3.80 days for the first dose among professionals receiving Comirnaty®, and 3.32 for Spikevax® (*P* value: .27; 95%CI: [-0.8, +1.55]). At the second dose, the mean was 2.86 for Comirnaty® and 2.59 for Spikevax® (*P* value: .4; 95%CI: [-0.9, +1.4]).

Regarding the demand for care, outcome, severity, and causality criteria for suspected ADR, there were no differences between the 2 groups, either with the first or second dose.

Table 3

Number of ADR according to dose and vaccine type.

	Comirnaty		Spikevax	
Number ADR 1st dose	156	20.5%	55	41.6%
Number ADR 2nd dose	461	60.6%*	36	29%**
Number ADR 1st and 2nd dose	145	19%*	41	33%**

*Calculated on 761 patients who received the 2 doses.
**Calculated on 124 patients who received the 2 doses.
ADR = adverse drug reaction.

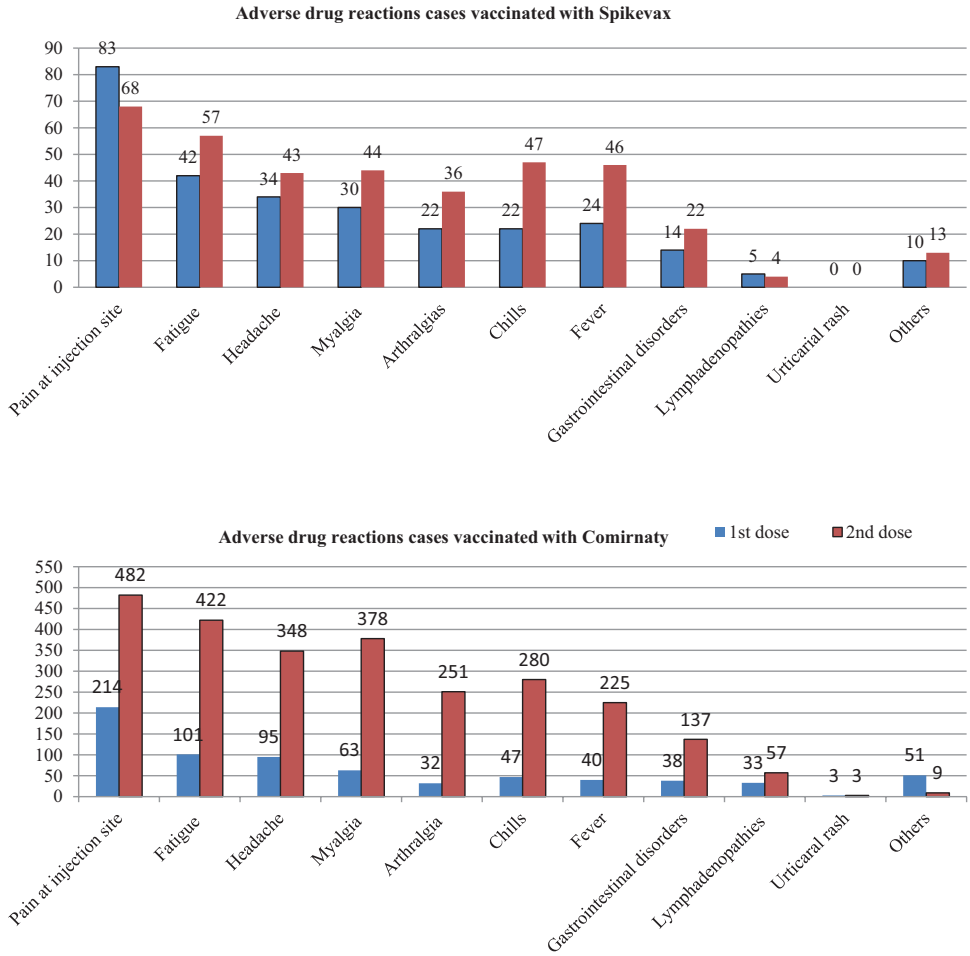

Figure 5. Most frequent adverse effects after 1st and 2nd dose.

3.6. Post hoc analysis: differences in suspected ADR between the first dose of Comirnaty® and the first dose of Spikevax®

The fact that a higher percentage of professionals with a history of COVID-19 received the Spikevax® vaccine could explain the higher frequency of ADR reported after the first dose of Spikevax® than with Comirnaty®. To corroborate this possible explanation, a post hoc analysis was carried out for suspected ADR after the first dose of the 2 vaccines, separating the professionals into groups with or without a history of COVID-19 (see Table 4). With regard to general (fatigue, headache, myalgia, arthralgia, chills, and fever) and gastrointestinal symptoms, the differences were greater among professionals with a history of COVID-19, but there were still a higher number of reports relating to the first dose among professionals who received the Moderna/Lonza vaccine and had not had COVID-19. However, regarding pain at the injection site, there was a greater difference among professionals with no history of COVID-19.

4. Discussion

The main results of this study showed that, in 3 months, 9549 professionals were vaccinated with 1 dose and 8169 with 2 doses. Suspected ADR were reported by 894 professionals, representing 11% of those vaccinated during that time period. A higher percentage of reports were associated with the second dose (77.2%) than with the first dose (44.4%). The majority of suspected ADR reported were those associated with SmPC. As seen in clinical trials,[16,17] pain at the injection site and general symptoms (fatigue, headache, and myalgia) are the most commonly reported ADR. These symptoms, also detected in clinical trials, appear more frequently after the second dose. In most cases, mild symptoms did not require medical assistance, and recovery was achieved in approximately 3 days.

Among the undescribed ADR, herpes simplex and herpes zoster were the most frequent notifications, as were dizziness and paresthesia. Post-marketing safety monitoring and reporting of undescribed suspected ADR are the most appropriate strategies for assessing less frequent adverse reactions associated with medicinal products and vaccines.[18] Hence, PhFVs at different health centers play a fundamental role in the generation of new signals. In recent months, we have observed important changes in the SmPC of some vaccines, as well as recommendations affecting specific population groups.[19]

Among professionals who had COVID-19, more suspected ADR were reported after the first dose than among those who had not had the disease. The number of general symptoms was also higher among the professionals with a history of COVID-19. However, the ADR profiles and prognoses were similar in both the groups. This information may be useful for adjusting vaccination strategies among different population groups.[20]

In the fourth pharmacovigilance report on COVID-19 vaccines published on April 9th, 2021, the 10 most frequently reported suspected ADR for both Comirnaty® and Spikevax® vaccines were pyrexia, headache, myalgia, pain at the injection site, discomfort, nausea, chills, arthralgia, fatigue, and lymphadenopathy. Although the percentages were different from those observed in our study, the ADR profiles were very similar. Regarding unknown ADR, the gastrointestinal ADR (diarrhea

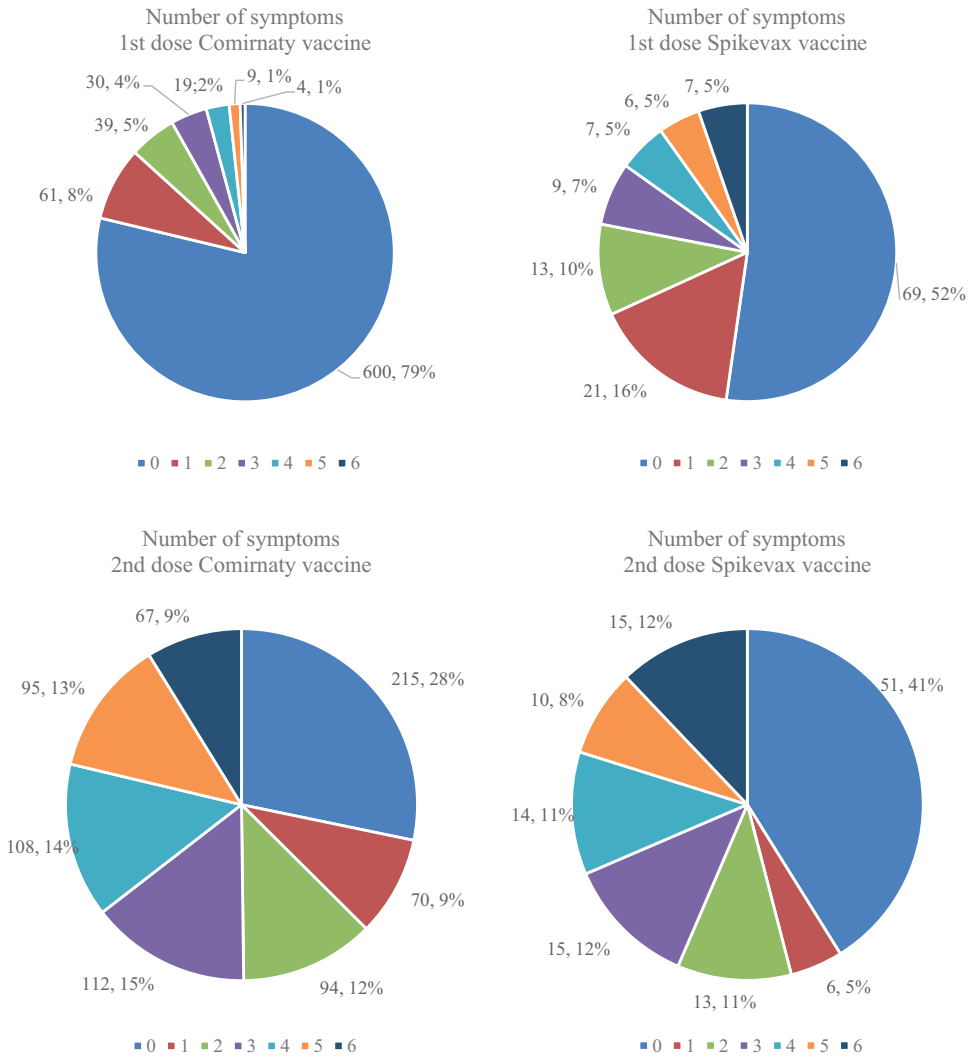

Figure 6. Number of symptoms according to vaccine type.

Table 4

Most frequent side effects after the 1st dose of the Comirnaty and Spikevax vaccines depending on whether professionals had a history of COVID-19 or not.

	No history of covid-19			History of covid-19		
	Comirnaty	Moderna	Difference	Comirnaty	Moderna	Difference
Pain at injection site	26	62.1	36.1	43.2	65.5	22.3
Fatigue	11	22.3	11.3	29.5	65.5	36
Headache	11	17.3	6.3	24	55.2	31.2
Myalgia	5.8	16.5	10.7	27.3	44.8	17.5
Arthralgia	3.3	6.8	3.5	11.4	51.7	40.3
Chills	5	6.8	1.8	16	51.7	35.7
Fever	3.6	6.8	3.2	18.2	58.6	40.4
Gastrointestinal disorders	4	8.8	4.8	11.3	17.2	5.9
Lymphadenopathies	2.8	5	2.2	16	0	-16
Urticarial rash	0.4	0	-0.4	0	0	0
Others	5.8	8.7	2.9	13.6	3.4	-10.2

The negative sign indicates the numerical superiority of the Comirnaty vaccine.

and vomiting) were the ones also detected in our study. However, other less common adverse events listed in the report, such as immune thrombocytopenia, were not observed in our study.[21]

In the publication of the report analyses received by the Vaccine Adverse Event Reporting System, 3908 ADR were collected in December 2020. The population included was similar to that included in our study, with an average age of 42 years, 80% women, and 95% referred to the vaccine developed by Pfizer. The most frequently described ADR in the publications were fatigue, pain, chills, headache, dizziness, and paresthesia.

This ADR profile is very similar to that of our study, in which dizziness and paresthesia were, in addition to the symptoms described in clinical trials.[8]

The Spikevax® vaccine rollout occurred later. Therefore, fewer professionals were referred to this vaccine, although the number of vaccines available in the hospital could also explain this difference. Among those who received Spikevax®, a higher proportion had a history of COVID-19. This could be justified by the later introduction of the Spikevax® vaccine and the fact that some professionals were waiting for the recommended time to elapse between disease and vaccine administration. On the other hand, the fact that the percentage of professionals with a history of COVID-19 was higher in the Spikevax® group could explain why ADR reports were more frequent after the first dose with Spikevax® than with Comirnaty®. However, post hoc analysis showed that the differences were greater for those with a history of COVID-19 when considering only general and gastrointestinal symptoms. Additionally, a greater number of reports after the first dose were maintained among professionals who received the Moderna vaccine, including those who did not have COVID-19. A review published by Meo et al, comparing the Comirnaty® and Spikevax® vaccines, also suggests that the latter presents a greater number of ADR, although the same authors affirm that these results could be accounted for by the heterogeneity of the studies, since no direct comparisons were available.[22]

Among the limitations of this study, it should be noted that these were suspected ADR reports made by professionals who had received the vaccine. Therefore, we cannot calculate the incidence or prevalence of adverse effects across the population or compare subgroups.

One limitation is that the reports were not completely spontaneous since, on the one hand, those vaccinated were invited to fill out a form in case of ADR at the time of administering the vaccine and, in addition, in the collection via the form there was a list with the known reactions and a free report section. This limitation may have been increased for 2 reasons: one being the great impact that the vaccination process has had in the media, which might induce the reporting of an already known suspected ADR profile; the other reason is that the suspected ADR were reported by professionals who worked together, so we cannot rule out a contamination phenomenon.

Another limitation is that the study population consisted of active professionals. This may have affected the age of the study population. No data were available for people over 69 years of age, and only 2 professionals were over 65 years of age.

The design of the study did not allow us to determine whether the differences found between the vaccines were due to confounding factors.

5. Conclusions

Most suspected ADR that appear after the administration of the vaccine against COVID-19 are those described in the SmPC. These were mild symptoms that did not require medical assistance and recovered in approximately 3 days.

Professionals with a history of COVID-19 filed more reports after the first dose.

The Spikevax® vaccine is associated with a higher number of suspected ADR after the first dose; however, we cannot rule out that this difference between the 2 vaccines may be due to confounding factors.

Author contributions

All the authors contributed to the conception and design of the study. Material preparation, data collection, and analysis were performed by [Dolores Rodriguez], [Pilar Ordoñez] ez, and [Roser Llop]. The first draft of the manuscript was written by [Dolores Rodriguez] and all authors commented on the previous versions of the manuscript. All authors have read and approved the final manuscript.

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