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Original Article

Adverse effects linked to COVID-19 vaccines among hospital staff in Rabat's Ibn Sina University Hospital in Morocco

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ABSTRACT

In order to study the post-authorization adverse reactions (AEs) of the COVID-19 vaccines currently authorized in Morocco, they were reported to the pharmacovigilance unit after the vaccination of health personnel at the Ibn Sina University Hospital Center in Rabat, Morocco, with the Covishield recombinant vaccine from AstraZeneca or the inactivated SARS-CoV-2 (Vero Cell) vaccine from Sinopharm. The objective is to study the adverse effects reported after vaccination with two vaccines against COVID-19. This study was conducted as a retrospective review, using the VigiFlow system and Medical Dictionary for Regulatory Activities (MedDRA) as a classification tool. The overall incidence of local and systemic adverse events in this study was 7.55%. It was observed that the nervous system was the most frequently affected organ by the Covishield vaccine and the inactivated Vero Cell vaccine (46.26% and 42.22%, respectively). These effects were mainly dizziness (57.64% and 47.36%), followed by headache (21.39% and 15.78%) and vagal reactions (5.24% and 23.68%). The second most reported class of AEs includes general disorders and infection of the injection site (29.49% and 18.88%). In this class we mainly find pain at the injection site (65.75% and 52.94%), influenza-like illness and malaise (5.47% and 11.76%). Finally, other classes of conditions have been notified, but with low incidences. A comparison of the AE profiles of the two vaccines revealed an overall similarity in AEs. Until the date of this work, exploration of the data has revealed no cases of death, no cases of thrombosis, or of allergic reaction.

KEYWORDS: COVID-19-vaccine, adverse reactions, inactivated vaccine, recombinant vaccine.

INTRODUCTION

The pandemic caused by Coronavirus-2 (SARS-CoV-2), has resulted in more than 185,291,530 cases of infections and more than 4,010,834 deaths worldwide as of July 8, 2021 [1].

Thus, in order to control and reduce the rapid spread of the disease, vaccines have been developed and administered on a large scale to populations. According to the World Health Organization (WHO), until the end of September 2021, 194 vaccines are in the preclinical development phase, 121 vaccines are in the clinical development phase, and 10 vaccines are in the clinical phase (phase four). Among, these vaccines, there are different vaccine platforms, including inactivated, viral vector, RNA, DNA, and other platforms [2].

In Morocco, the vaccines used as part of the national COVID-19 vaccination campaign, during the period considered for this study are the Covishield vaccine from AstraZeneca and the

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inactivated Vero Cell vaccine from Sinopharm. AstraZeneca COVID-19 Vaccine contains Chimpanzee Adenovirus encoding the SARS-CoV-2 Spike Glycoprotein (ChAdOx1-S), not less than 25 × 108 infectious units (Inf.U), produced in genetically modified human embryonic kidney (HEK) 293 cells and by recombinant DNA technology [3]. Sinopharm's product is an inactivated vaccine called SARS-CoV-2 (Vero Cell). Upon issuance of emergency use authorizations (EUAs) for both vaccines, notification of adverse events (AEs) occurring after administration of these vaccines was required; close monitoring for at least 15 minutes was formally required after vaccination [4]. COVID-19 vaccines, like any vaccine, can cause side effects, and those reported from COVID-19 vaccines have been mostly mild to moderate and have not lasted more than a few days. Typical side effects include pain at the injection site, fever, fatigue, headache, muscle pain, chills, and diarrhea [5].

In Morocco, health workers were among the first categories to benefit from vaccination against COVID-19. As soon as the vaccination of the staff of the Ibn Sina University Hospital Center (CHU) in Rabat, Morocco was launched, a pharmacovigilance unit was set up to ensure the collection and processing of notifications of adverse reactions.

Thus, the aim of this work is to study the adverse effects (types, incidence, time of onset, severity, evolution, etc.) post-authorization, reported to the pharmacovigilance unit after the vaccination of health workers at the Ibn Sina University Hospital, Rabat, in Morocco, against COVID-19 disease with the Covishield recombinant vaccine from AstraZeneca or the inactivated SARS-CoV-2 (Vero Cell) vaccine from Sinopharm.

MATERIALS AND METHODS

Study period

January 28, 2021 to May 30, 2021.

Method

A retrospective study examining self-reported symptoms, after receiving the first and/or a second dose of one of the two vaccines; the reported symptoms were verified, confirmed, and recorded or officially documented by the Pharmacovigilance investigators of the vaccination campaign.

Vaccines administered

The inactivated vaccines are called SARS-CoV-2 Vero Cell vaccine, manufactured by the Sinopharm laboratory, and the Covishield vaccine (recombinant ChAdOx1-S); the latter is a vaccine manufactured by the laboratory Verity Pharmaceuticals and Serum Institute of India (SII) in collaboration with AstraZeneca [6].

Data source

Based on the system provided by the Uppsala Monitoring Center (VigiFlow). Individual Case Safety Reporting (ICSR) systems are available in the National Pharmacovigilance Centers of the WHO International Medicines Surveillance Program. VigiFlow supports collection, processing, and sharing of ICSR data to facilitate efficient data analysis. VigiFlow is compatible with the international ICH E2B standard and uses international terminology from the Medical Dictionary for Regulatory Activities (MedDRA). We thus obtained a database of adverse events following immunization (AEFI), which provides a variety of information, such as: age, sex, date of onset, name of vaccine administered, adverse event, seriousness, progress, and other information. However, spontaneous reports may not always have all the information for the reasons we have mentioned as 'not specified' in our results.

Study inclusion criteria

All potential cases of adverse reactions occurring within 24 hours of vaccination or later.

Data processing

The Excel spreadsheet software was used for the calculation and analysis of the data and the MedDRA classification of the VigiFlow system was used to group the reported adverse reactions by etiology ($p < 0.005$).

RESULTS

During the study period, 8,098 doses were administered to health workers at Rabat's Ibn Sina University Hospital. With 612 cases of

notification of adverse reactions after vaccination, the overall incidence of local and systemic adverse events requested in this study was 7.55%. The ages of those vaccinated varied between 22 and 69 years (median 45.5 years), although forty-two cases were not reported. The incidence of AEs in women was much higher than the incidence in men, with 85.94% versus 14.05%, respectively. The side effects appeared between one and nine days after the injection. In some cases, the time to onset was up to 15 days after the injection (median 7.5 days). 86.27% of people vaccinated reported AEs after the first dose of the vaccine, while 13.72% reported AEs after the second dose. For the Covishield AstraZeneca vaccine, 95.56% of the cases were not serious. However, 4.4% of the cases were not specified. While 93.25% experienced a favorable outcome, 4.62% were in the process of recovery at the time of notification. The trend of 1.9% was not specified in the notification report. For Sinopharm's VeroCell vaccine, 99% of cases were not serious, with only 1 case of unspecified severity. In terms of evolution, 72% of cases recovered, while 24.73% were recovering at the time of notification, 1% was not cured, and 2% did not specify. Of the total cases reported during the study period, 84.8% of cases were reported after injection of the Covishield AstraZeneca vaccine and 15.19% of cases were reported after injection of the Vero Cell (Sinopharm). The comparative distribution of cases, according to the classification of adverse reactions according to MedDRA is shown in Figures 1, 2, and 3.

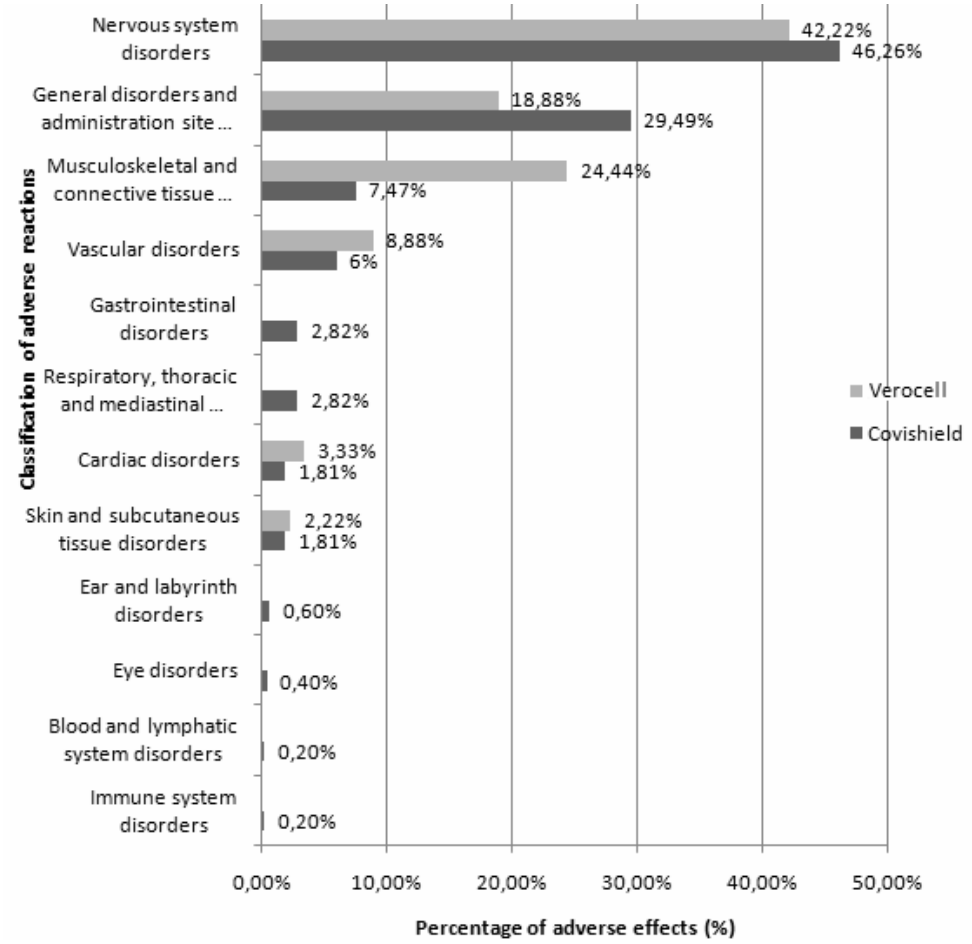

Figure 1. Comparison of reported adverse reactions following vaccination with Sinopharm vaccine and Covishield AstraZeneca vaccine according to MedDRA classification.

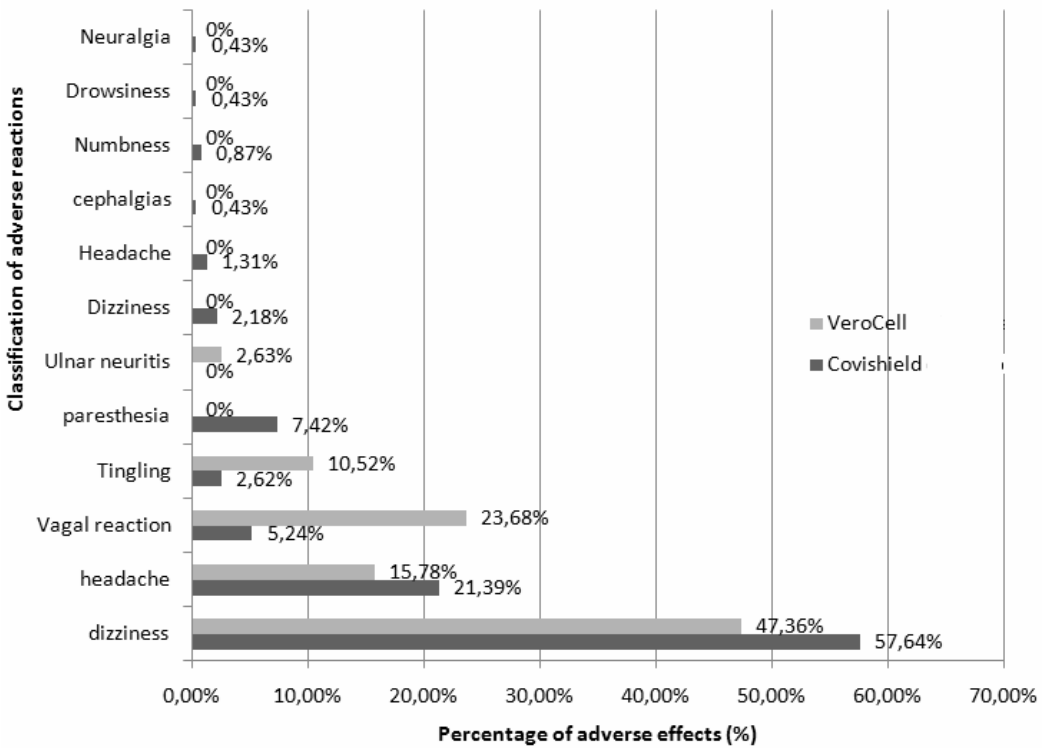

Figure 2. Distribution of nervous system disorders notified following vaccination with Sinopharm's VeroCell vaccine and AstraZeneca's Covishield vaccine.

DISCUSSION

Among the vaccinated health workers, we noted a predominance of women in our study series, 85.94% of women against 14.05% of men. This predominance was also observed in a study in the USA [7], and in Indonesia, with the Sinovac COVID-19 vaccine [8]. Since the turn of the century, women hold 76% of all health care jobs [9]. The side effects reported and treated in our study were more frequent after the first dose than the second. This has also been reported in studies after vaccination with Moderna vaccine and Pfizer vaccine against COVID-19 [10, 11]. In contrast, the CDC recently announced that AEs after the second dose of vaccine may be more serious than those after the first dose.

The Covishield recombinant vaccine

In our study, the highest incidence was that of disorders of the nervous system (46.26%), especially with the AstraZeneca vaccine. These effects were mainly dizziness (26.6%), followed by headache (9.89%). On the other hand, for other vaccines such as the Pfizer and Moderna vaccines, post-authorization reports say that localized reactions, in particular skin reactions, are the most frequent AEs [10, 12, 13]. As globally, in the United States, the new vaccine-based immunization program has generated many ongoing apprehensions, questions, and assumptions about the safety issues of new recombinant vaccines, among health workers and the general population [14]. On the one hand, as for all vaccines, vaccines against COVID-19 have AEs, as mentioned on their summary of product characteristics (SPCs). On the other hand, the list of symptoms mentioned in the SPC of the Covishield vaccine [11] is narrower compared to the results of our study. Certain effects reported in our study were not reported on the SPC of the Covishield vaccine, such as certain heart disorders, certain vascular disorders, certain eye conditions, certain immune disorders, certain ear and labyrinth disorders, and certain respiratory, thoracic, and mediastinal disorders (Figure 1). These AEs were also reported in a study in the USA performed on

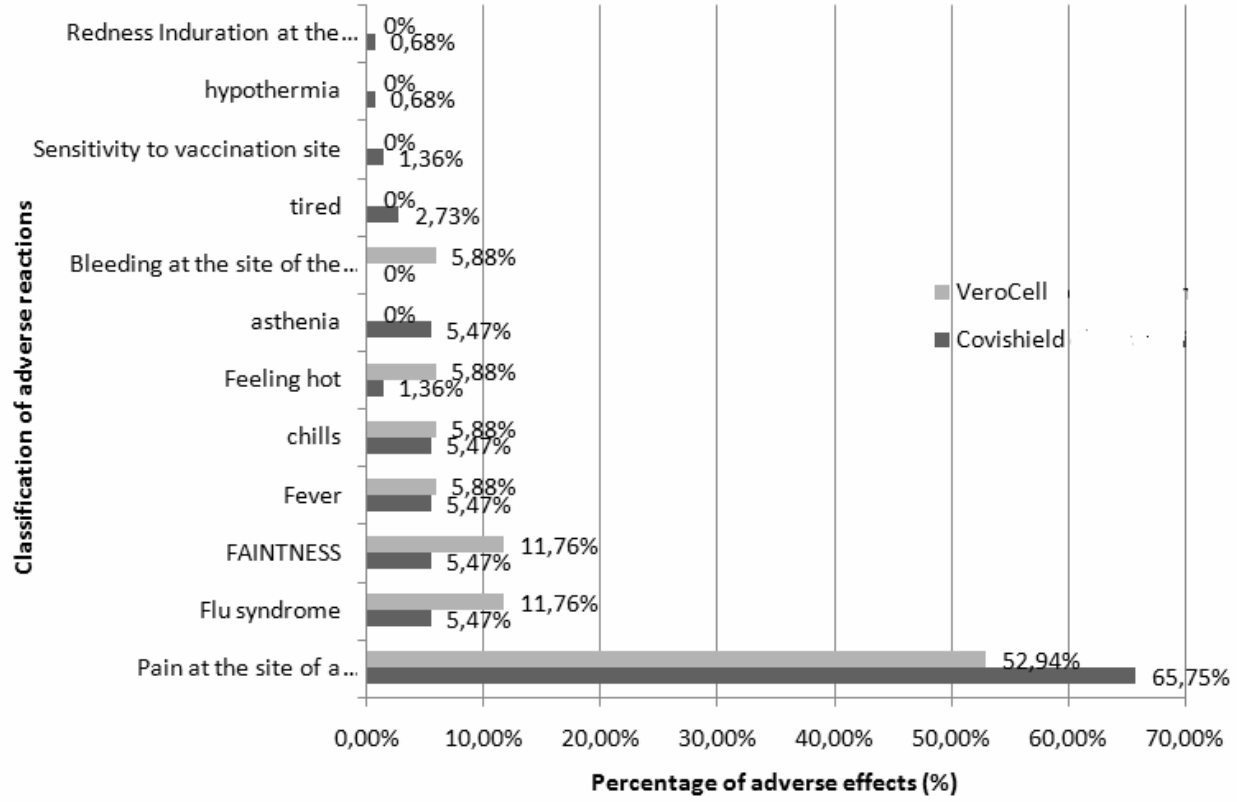

Figure 3. Distribution of general disorders and injection site abnormalities notified following vaccination with Sinopharm's VeroCell vaccine and AstraZeneca's Covishield vaccine.

COVID-19 vaccine with ARNm BNT162b2 (Pfizer-BioNTech) [14]. It should be noted that, in our study, the notified effects did not reveal any serious safety problem threatening the lives of people vaccinated with the Covishield recombinant vaccine. This was also observed in a study of self-reported AEs with mRNA-1273 vaccine (Moderna) in healthcare workers, which showed a broad spectrum of symptoms, most of the symptoms were not life-threatening, and high acceptance of the vaccine among health workers [4]. It was noted that during the period of this study, data mining did not reveal any deaths or thrombosis or a severe allergic reaction. Although, one case of allergic reaction was reported in the notification reports processed in this study with the Covishield recombinant vaccine, on the notification it was clarified that this was a non-serious case with a favorable outcome. Morocco's Ministry of Health devotes special attention to cases of allergies, and for this it recommends that all vaccinated people be observed for at least 15 minutes after receiving the vaccine under medical supervision, with emergency kits available at the vaccination site in case it is necessary [4]. These recommendations are also endorsed by the WHO and the CDC [15, 16].

Sinopharm's inactivated Vero Cell vaccine

The results of our study demonstrated that the majority of reported AEs were general disorders and administration site abnormalities, skin and subcutaneous tissue disorders, cardiac disorders, vascular disorders, musculoskeletal and connective tissue disorders, and nervous system disorders. In a survey carried out in Indonesia among hospital workers vaccinated with the inactivated Sinovac vaccine, similar effects were reported, such as general disorders and administration site abnormalities, nervous system disorders, musculoskeletal disorders. On the other hand, other side effects have been reported with

the inactivated Sinovac vaccine [8], but have not been notified for Sinopharm's inactivated Vero Cell vaccine, such as disorders of the lymphatic system, disorders of the respiratory system, gastrointestinal disorders, and anaphylactic reactions. Similarly in India, after the use of an inactivated BBV152 vaccine, the most frequently reported AEs were general disorders and administration site conditions (swelling, frisks, fever, fatigue or malaise), nervous system disorders (headache, anorexia), gastrointestinal, musculoskeletal, and connective tissue disorders (body ache, myalgia), gastrointestinal disorders (nausea or vomiting, and diarrhea), and skin and subcutaneous tissue disorders (generalized rash) [17]. In addition, in a phase 1/2 clinical trial in China on an inactivated COVID-19 vaccine, CoronaVac, the most common side effects were pain at the injection site (9% mild or moderate), fever (3%), headache, and mucosal rash, and no serious vaccine-related adverse reactions were recorded [18]. In another phase 3 trial carried out in the United Arab Emirates, Bahrain, Egypt and Jordan, on two inactivated vaccines WIV04 and HB02, both developed by China, the results collected showed that the most common adverse effects in the WIV04 group, and the HB02 group were injection site pain (24.3%, 19.4%) followed by headache (12.9%, 13.1%). Most of the side effects were mild in severity (grade 1 or 2) and were transient and self-limiting, without requiring any special treatment [19]. Thus, inactivated vaccines are well established, and they may provide benefits in a variety of distinct populations, including those with varying degrees of immune weakening [20].

Comparison of the two vaccines

The comparison of the adverse reaction profiles reported after administration of the two vaccines shows a similarity at the level of certain categories of AEs including disorders of the nervous system, vascular disorders, and skin and subcutaneous tissue disorders. In fact, while the incidence of some AEs varied, the incidence of general disorders and administrative site abnormalities was higher. On the other hand, we noted a difference in the incidence of other categories of AEs, such as the incidence of general disorders and anomalies of the administration site, which were higher with the Covishield vaccine, and the incidence of musculoskeletal and connective tissue disorders, vascular disease, and heart disease, which were higher with Sinopharm's Vero cell vaccine. In contrast, some AEs have been reported only with the Covishield vaccine, like gastrointestinal, respiratory, thoracic, and mediastinal conditions, ear and labyrinth conditions; eye, hematology, lymphatic system, and immune system conditions. Our results are similar to a study in India, where researchers found BharatBiotech's inactivated BBV152 vaccine to be safe and less reactogenic than BNT162b2 mRNA vaccine (Pfizer-BioNTach) and mRNA-1273 (Moderna) [21].

Limitations of the study

Most of the symptoms reported above were reported early in the post-vaccination phase of the vaccine. The latent effects of these vaccines were not studied or included in this study. The severity of each symptom was not assessed quantitatively in the study. In the absence of data on the baseline rates for each adverse event, it was not possible to compare the incidence rates obtained with those expected during a public vaccination. Pre-existing chronic medical conditions may have contributed to these side effects, or they could be a coincidence of new underlying medical conditions that were not related to the vaccine. An analysis of the causality assessments could not be carried out due to the lack of certain information on the pharmacovigilance notice sheet. Finally, there is no clear indication that the vaccine had a confirmed role in the occurrence of these adverse effects.

CONCLUSION

In this study series, disorders of the nervous system followed by general disorders and abnormalities at the injection site were the most reported side effects. The results of this work are generally similar to those reported in other international studies. No serious adverse events or deaths were reported during the period considered for this study. In a context of security and vigilance, it would seem that the two vaccines used did not represent a danger until the time of this study.

CONFLICT OF INTEREST STATEMENT

All authors declare no conflicts of interest.

ABBREVIATIONS

AEs	:	Adverse reactions
AEFI	:	Adverse events following immunization
CDC	:	Centers for Disease Control and Prevention
CHU	:	University Hospital Center
DNA	:	Deoxyribonucleic acid
EUA	:	Emergency Use Authorizations
ICSR	:	Individual Case Safety Reporting
MedDRA	:	Medical Dictionary for Regulatory Activities
RNA	:	Ribonucleic acid
SPC	:	Summary of Product Characteristics
WHO	:	World Health Organization

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