Original Research / Orijinal Araştırma

The Sideeffects of Covid-19 Vaccine (Coronavac): A Study In A Province of Türkiye

Covid-19 Aşısının (Coronavac) Yan Etkileri: Türkiye'nin Bir İlinde Yapılan Bir Araştırma

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Abstract

Objective: The discovery of vaccines during the COVID-19 pandemic was encouraged to establish immunity and decrease the effects of the virus. Vaccines, like any other medicine, include the possibility of side effects. This study was carried out to categorize the side effects and to show that no severe side effects developed. In this study, we aimed to examine the patients who came to the emergency department with side effects after administering the inactivated vaccine. Material Methods: In this study, between January and March 2021, healthcare workers and people over 80 who applied to the emergency department after developing a side effect after administering the Coronavirus disease-2019 (COVID-19) vaccine were included. Results: In the study, 82 (82.8%) were healthcare professionals, and 17 (17.2%) were in the over-80 age group. The most common side effect was COVID-like findings (47.5%). While the rate of applications to the emergency department after the first dose of vaccination was69.7% (n=69), it was observed that it decreased to 30.3% (n=30) after the second dose of the vaccine. Conclusion: In general, post-vaccination side effects are tolerable and not life-threatening. Furthermore, the risk of becoming infected with the virus post-vaccination is lower. Therefore, hesitation to vaccinate may cause more risk.
Keywords: COVID-19, CoronaVac, vaccine, side effect.

Özet

Amaç: Koronavirüs pandemisi sürecinde aşıların keşfi, bağışıklık gelişmesi ve virüs etkilerinin azalması açısından umut olmuştur. Ancak her tedavi yönteminde olduğu gibi, aşıların da yan etki oluşturma riski mevcuttur. Gelişen yan etkileri kategorize etmek ve ciddi yan etki gelişmediğini göstermek amacıyla yapılan bu çalışmada; inaktive aşı uygulamasında gelişen yan etkilerle acil servise gelen hastalar incelenmeye çalışıldı. Materyal Method: Çalışmaya Ocak-Mart 2021 tarihleri arasında, COVID-19 (Coronavirus disease 2019) aşısı (Sinovac-CoronaVac) uygulanan sağlık çalışanları ve 80 yaş üstü kişilerden, yan etki gelişip acil servise başvuran hastalar dahil edilmiştir. Bulgular: Çalışmaya dahil olan hastalardan 82'si (%82,8) sağlık çalışanı, 17'si (%17,2) ise 80 yaş üstü grupta idi. En sık COVID benzeri bulgular (%47,5) saptanmıştır. İlk doz aşı sonrası acil servis başvurularının hızı %69,7 (n=69) iken, 2. doz aşı sonrası başvuruların %30,3'e (n=30) gerilediği gözlenmiştir. Sonuç: Genel olarak aşı sonrası yan etkiler tolere edilebilir düzeydedir ve hayati risk oluşturmamaktadır. Ayrıca aşılanma sonrası virüs ile enfekte olma riski düşüktür. Bu yüzden aşı tereddütü daha fazla risk alınmasına sebep olabilir.
Anahtar kelimeler: COVID-19, CoronaVac, aşı, yan etki.

Geliş tarihi / Received: 30.07.2022 Kabul tarihi / Accepted: 02.01.2023

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Guven O, Kasikeman O, Selcuk H, Demireller M, Kurt BF. The Sideeffects of Covid-19 Vaccine (Coronavac): A Study In A Province of Türkiye. TJFMPC, 2023;17(1): 87-93

DOI:10.21763/tjfmpc.1151226

Introduction

The Coronavirus disease- 2019 (COVID-19) pandemic has infected over 760 million people and resulted in the deaths of over 6 million people worldwide. Although numerous medications have been proven useful for patients, it was agreed that the most effective technique was preventing the virus because no definitive therapy could be established. In addition to individual protection methods, vaccine development studies have been accelerated in many countries, and next-generation vaccines have been developed (Table 1)[1]. Inactivated vaccines produced by the classical method and new-generation RNA vaccines have been introduced to the market together. Countries tried to produce their vaccines and it was aimed to spread vaccination all over the world.

Table 1: Types of vaccines developed for COVID-19

- Vaccines containing the inactivated virus that does not cause disease but produces an immune response (Inactivated vaccines)
- Vaccines containing the weakened virus that does not cause disease but produce an immune response (Live attenuated vaccines)
- Protein-based vaccines that use protein fragments that mimic the structure of the COVID-19 virus to generate an immune response safely
- Viral vector vaccines using non-disease viruses carrying RNA fragments of the COVID-19 virus to generate a safe immune response
- m-RNA and DNA vaccines are a state-of-the-art approach that uses genetically-engineered RNA and DNA fragments to produce proteins inducing an immune response safely.

The vaccination process in our country started in January 2021 with the inactivated SARS-CoV-2 (Sinovac-CoronaVac Vero Cell) vaccine produced in China, and other vaccines have been tested as well. Firstly, healthcare professionals and those over 80 were considered the riskiest group and they were vaccinated. Then the age groups were found to be at lower risk or with a milder course of infection, respectively. In the studies, the most common side effects after mRNA vaccination were pain and fatigue at the injection site. This situation was most common after the second dose[2]. This may have caused vaccine hesitations. However, no life-threatening side effects were observed, particularly among those vaccinated with conventional vaccines. In this study, we tried to show emergency department (ED) data that tolerable side effects can occur for people afraid of the vaccine's side effects.

Material Methods

The local ethics committee approved this research (PR0300R01/6). The vaccination records of 5383 people, male and female, who were vaccinated with CoronaVac among healthcare professionals in all age groups and patients over the age of 80 between January 14, 2021(the date of vaccination in our country) and March 14, 2021, were examined. In this population, the files of 99 patients who applied to the ED with the complaint of side effects after the 1st dose or the 2nd dose vaccination were scanned. Findings such as demographic characteristics, how long after vaccination the patient applied to the ED, complaints for admission, and whether the patient received inpatient treatment or not were noted. Since our study was retrospective and in file scanning, patient consent was not obtained, and the information was anonymised.

In the descriptive statistics of the data, with the SPSS 28.0 program, mean, standard deviation, median lowest, highest, frequency and ratio values were analyzed, and the chi-square analysis was used to examine the distributions between groups.

Results

Of the patients in the study, 55 (55.6%) were female, and 44 (44.4%) were male. Of these patients, 82 (82.8%) were healthcare professionals, and 17 (17.2%) were in the group over 80. The mean age of all patients was 61. 3±19.1 years. 69.7% (n=69) had a history of chronic disease. Those who received hypertension treatment were in the majority with 48.5% (Table 2) (Some of the patients had more than one comorbidity). Comorbid disease was found in 49 (71%) of the patients who developed side effects after the 1st dose and in 19 (63.3%) of the patients who had side effects after the 2nd dose of vaccine. No side effects were observed in the same patient after the first and second dosages.

Table 2: **Classification of chronic diseases of the patients with side effects**

	n	%
Hypertension	48	%48.5
CHF/ Heart valve disease	18	%18.2
Neurologic	5	%5.1
Endocrinologic	32	%32.3
Other	13	%13.1

CHF: Chronic heart failure
Other: Chronic lung disease, cancer, orthopaedic diseases, blood diseases, ophthalmologic diseases, etc.

COVID-like symptomswere cough, fever, malaise, joint pain; cardiac symptomswere tachycardia, hypertension, hypotension, arrhythmia; neurologicalsymptoms were neurological deficit, syncope, dizziness, headache; GIS (Gastrointestinal)symptoms were diarrhoea, abdominal pain, nausea, vomiting; skin lesionswerepain at the injection site, itching, redness, rash; and respiratory symptomswere dyspnea, hypoxia.
COVID-like symptoms were the most frequent (47.5%) among the vaccine side effects (Table 3). It was determined that patients with this complaint applied to the ED within an average of 3.2±2.1 days after vaccination.

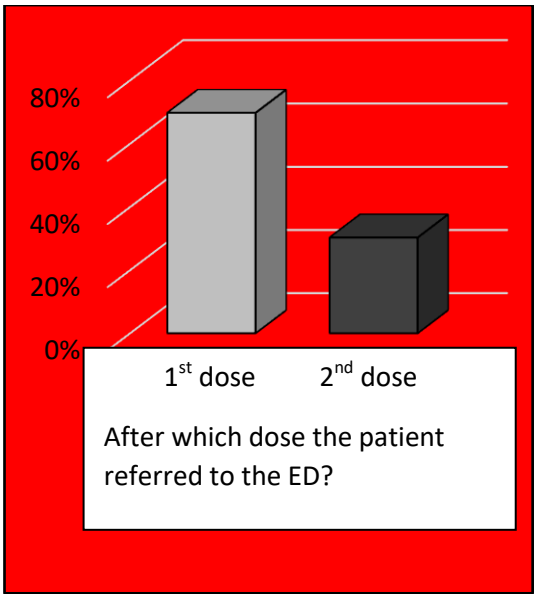
Table 3: Symptoms noticed after vaccination

	n	%
COVID-like	47	% 47.5
Cardiac symptoms	18	%18.2
Neurological	12	%12.1
GIS symptoms	12	%12.1
Skin lesions	5	%5.1
Respiratory symptoms	5	%5.1

GIS: gastrointestinal system

While the rate of applications to the ED after the first dose of vaccination was 69.7% (n=69), it was observed that it decreased to 30.3% (n=30) after the second dose of the vaccine (Figure 1). Sixty (86.9%) of the patients who applied after the 1st dose of vaccination and 22 (73.3%) of those who applied after the 2nd dose of vaccination were healthcare professionals.

Figure 1: ED admission rate by vaccine dose



Twelve patients (12.1%) were reported to admit to the ED within 24 hours of vaccination, and 13 patients (13.1%) within 48 hours. 7 patients (7.1%) were hospitalized, and the mean age of these patients was 80.3±10.0. It was determined that cardiac symptoms developed in 4 of them, neurological symptoms in 2 patients and respiratory symptoms in 1 patient. Three (42.8%) of these patients were healthcare professionals (Tables 4 and 5). All patients were reported to have been discharged following treatment.
Furthermore, 4 people had a history of COVID-19 before getting vaccinated (4%). It was determined that 3 of these patients developed a COVID-like side effect (75%) and one of them developed cardiac side effects (chest pain) (25%).

Table 4: Comparison of hospitalized and discharged patients with regard to comorbidities and symptoms

	Hospitalized Mean±SD Median n %	**Discharged** Mean±SD Median n %	**p**
Age	80.3±10.0 84	59.8±18.9 66	**0.002 (m)**
Gender F	3 42.9%	52 56.5%	
M	4 57.1%	40 43.5%	0.483 (X^2)
***Comorbidity**			
HT	7 100.0%	41 44.6%	**0.005 (X^2)**
CHF/Heart valve disease	4 57.1%	14 15.2%	**0.002 (X^2)**
Neurologic			
Endocrinologic	1 14.3%	4 4.3%	0.312 (X^2)
Other	3 42.9%	29 31.5%	0536 (X^2)
App. dose	1 14.3%	12 13.0%	1.000 (X^2)
1st			
2nd	5 71.4%	64 69.6%	
***Symptoms noticed after vaccination**	2 28.6%	28 30.4%	0.919 (X^2)
COVID Like			
Cardiac symptoms	0 0%	47 51.1%	**0.009 (X^2)**
Neurological symptoms	4 57.2%	14 15.2%	**0.011 (X^2)**
GIS symptoms	2 28.6%	10 10.9%	0.200 (X^2)
Skin lesions	0 0%	12 13%	0.593 (X^2)
Respiratory symptoms	0 0%	5 5.4%	1.000 (X^2)
	1 14.3%	4 4.3%	**0.039 (X^2)**

F: Female, M: Male, SD: Standard deviation, HT: Hypertension, CHF: Chronic heart failure, GIS: gastrointestinal system, Other: Chronic lung disease, cancer, orthopaedic diseases, blood diseases, ophthalmologic diseases, etc., App: Application
**X: There are more than one comorbidity and symptoms in the same patient*
m: Mann-Whitney U test, X^2: Chi-square test

Table 5: Characteristics of inpatients

Patients' number	1	2	3	4*	5	6*	7*
Age	87	95	84	69	85	69	73
Gender	M	F	F	M	M	M	F
Comorbidity	+	+	+	+	+	+	+
App. dose	1	2	2	1	1	1	1
App. period	3	1	3	2	2	4	2
Side-effect	Tachycardia	Tachycardia	Arrhythmia	Bell palsy	Arrhythmia	Dyspnea	Dizziness + Pre-syncope

X: Healthcare professionals, App: Application*

Discussion

During the COVID-19 pandemic, most developed countries encouraged scientists to use resources to develop vaccinations. Before clinical trials were completed, vaccines began to be tested in human volunteers in Phase 3, with emergency approval. Over ten types of vaccines were produced today, and none of them had severe short-term results.[3-6]

Compared to other types of vaccines, inactivated vaccines are more reliable in humans because they are produced with more standard technology that is easy to store and transport[7]. A study by Al-Kaabi et al. determined that two inactivated COVID-19 vaccines were effective at 78.1% and 72.8%[8].

In a study by Elnaem et al., the population vaccinated with three different types of vaccines was examined. The lowest side effects were seen in people vaccinated with CoronaVac and in the first dose of the vaccine[9]. In a study by Rerknimitr and al. with CoronaVac and Vaxzevria, post-vaccination cutaneous lesions were examined. It was found that urticaria lesions were more common in patients vaccinated with CoronaVac[10]. In this study, skin lesions developed, but COVID-like and heart symptoms were more frequent.

In a study by He et al., it has been reported that local and systemic side effects are less common in inactivated vaccines than in other vaccine types. However, the capacity of inactivated vaccines to induce a T-cell response that secretes IFN-γ was lower than other vaccines[11]. Therefore, vaccination with an inactivated vaccine may be a good option in the population over 80 years of age and with comorbid disease. Still, sequential vaccination may be required since its effectiveness will be shorter.

In this study, among patients who applied to the ED after vaccination, the rate of patients who developed side effects after vaccination was 1.83% (vaccinated n=5383, n=99 who were referred to the ED). According to this result, a lower risk is taken in the population at risk, incomparable to the problems that will occur during the disease.

In the literature, there are data on post-vaccination outcomes, mainly among health professionals and vaccine hesitancy. In the study by Riad et al., healthcare professionals vaccinated with inactivated vaccines in Turkiye were examined. COVID-like side effects were found at the highest rate. These findings were more common in the female gender. It was observed that these side effects disappear on average in 3 days[12]. In this study, in general, and in most of the patients referred to the ED within 24 hours, COVID-like side effects were detected. In this case, it can be said that requests to the ED have increased due to the fear of being infected by COVID-19 after vaccination. Additionally, this is not an unexpected outcome, as this study coincided with the winter season when influenza infection is common. In addition, unlike the studies mentioned, this study, which includes data from the population of the most at-risk age group, is enlightening for the literature.

In the Tanrıöver et al.'s study with inactivated COVID vaccine and placebo, it was observed that a serious side effect (allergic reaction) developed in 1 patient in the vaccine group after 24 hours, and this symptom regressed within 2 days[13]. In a study by Govaert et al., systemic and local side effects were compared in the two groups vaccinated with inactivated influenza vaccine and placebo. Although local side effects were higher in the vaccine group, systemic side effects were similar in both groups. Headache and fatigue were the most frequent systemic side effects[14]. Based on this outcome, systemic side effects may not be vaccine-related. In this study, the headache was accepted as a neurological symptom. Despite this, COV-like symptom, such as fatigue, was among the most common.

In the study, the rate of ED admission after the first dose of vaccine is higher than the rate after the second dose of vaccine. In people who have been vaccinated for the first time, it may be that every symptom (even symptoms due to chronic diseases) is thought to be due to the vaccine, at a time when vaccine side effects are not known.
In the study by Tissot et al. on the side effects after the new generation mRNA vaccine, the rate of development of side effects in patients who have had COVID-19 before has been found to be higher than in those who have not had COVID-19. It has been emphasized that individuals with high antibody levels may have developed a rapid immune response[15]. In another study investigating side effects in people under 23 who received the mRNA vaccine, local side effects were seen after the 1st dose, and systemic side effects (most COVID-like symptoms) were seen after the 2nd dose[16]. In this study, on the contrary, it has been determined that fewer side effects develop in patients who have had COVID-19 before and that side effects are more common after the 1st dose. In this case, inactivated vaccines can be safely preferred among young people and those without a history of COVID-19.
Interferon type 1 (IFN-1) is considered to cause symptoms such as headache and fatigue, which are frequently seen in next-generation vaccines other than inactivated vaccines[17]. Inactivated vaccines may be preferred by people who have such chronic symptoms.
In general, the elderly has lower immunity. While young people are less likely to suffer serious consequences and die from illness, they tend to be infected more frequently, remain infected longer, and thus become vectors for transmission to the elderly who are not adequately protected by the vaccine[18]. Therefore, vaccination of the elderly population, a vulnerable group, and healthcare professionals exposed to viral load may have saved time during the pandemic. However, suppose the vaccine proves significantly more effective in children, and children represent an important vector for the spread. In that case, vaccination policies may need to prioritize children over the elderly[19]. In this case, an inactivated COVID-19 vaccine with no severe side effects is a good alternative.

Limitations of the study

There are some limitations in the study. In the province where the study was conducted, most elderly patients were vaccinated at home. The healthcare professional received the vaccine from the hospital's outpatient clinic. Therefore, when adverse events occur after vaccination, the number of applications by healthcare professionals can be high. In general, local symptoms such as post-vaccination skin damage are acceptable to the patient. Therefore, it is possible that these side effects were not reported in the home-vaccinated group. However, no significant complications were reported in this population as well.

Conclusion

Since this study included the first vaccination data in our country and was conducted in the largest and only hospital in the province, it can be considered a good example, and the data obtained should be included in the literature.
No life-threatening adverse effects were found in this study. No severe findings were detected in the population likely to have a severe course of Corona diseases, such as healthcare workers and over 80. All results were tolerable or treatable. In general, the side effects after vaccination are not more significant than the complications associated with COVID-19. That's why getting vaccinated is so important.
Despite the rapid development of vaccines during the pandemic, minimal side effects are an outstanding achievement. It can be predicted that as a result of detecting and transparently explaining the side effects that occur or may occur with all types of vaccines, vaccine hesitancy will decrease, and the effectiveness of the COVID-19 virus will decrease. Multi-center studies on long-term adverse events of vaccines are necessary.
Although vaccination provides extensive individual protection, it was observed that the efficacy against the varieties observed at the time of this article was low. Therefore, developing sequenced vaccines and next-generation vaccine varieties is necessary.

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