Manifestations of adverse events post Sinovac vaccine immunization at Wirasakti Hospital, Kupang

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Abstract

Background. Since it was first discovered, COVID-19 has spread worldwide and has been declared a pandemic by the World Health Organization. One of the various efforts made to prevent the spread of COVID-19 is the development of the COVID-19 vaccine. One of the vaccines developed and used by the Indonesian government is the Sinovac vaccine. However, like vaccines in general, there are always vaccine safety problems which are better known as adverse events following immunization (AEFI).

Objective. The purpose of this study is to determine the AEFI manifestations that occurred in Sinovac vaccination participants at Wirasakti Hospital, Kupang.

Methods. The sample included 51 people, who later became known as research subjects. The criteria for vaccine recipients and instructions for recording AEFI refer to the technical guidelines issued by the Ministry of Health, namely the Decree of the Director General of Disease Prevention and Control number HK.02.02/4/1/2021 regarding technical instructions for implementation of vaccination in the context of combating pandemic COVID-19.

Results. The results showed that out of 198 vaccination participants, 15 of them had AEFI and those who had AEFI were women. The AEFI manifestations that occur are dizziness, palpitations, shortness of breath, cramps in the hands, and trembling hands. All AEFI that occurred are non-serious in nature.

Conclusion. Sinovac vaccine is relatively safe to use because only a small proportion of respondents (29.4%) have AEFI.

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Introduction

The first COVID-19 was reported in Wuhan, Hubei Province, China in December 2019. The source of transmission of this case is still unknown, but the first case was linked to a fish market in Wuhan.[1] Between December 18 to December 29, 2019, five patients were treated with acute respiratory distress syndrome.[2] This disease increased rapidly from December 31, 2019, to January 3, 2020, marked by the reported 44 cases. In less than a month, the disease has spread to other provinces in China, Thailand, Japan, and South Korea.[3] On 12 March 2020, the World Health Organization (WHO) declared COVID-19 a pandemic.[4]

COVID-19 is a disease that attacks the respiratory system in humans and is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[5] This disease has spread widely and has infected nearly 99.8 million people worldwide. The cumulative number of people who have been infected with COVID-19 globally on October 1, 2021, has reached 234,723,525 cases, with 18,391,279 active cases, 4,800,629 deaths, and 211,531,617 recoveries.[6] Indonesia alone has 4,216,728 total cases with 34,867 active cases, 4,039,835 recoveries, and 142,026 deaths as of October 1, 2021.[7]

The rapid spread of COVID-19 and limited effective treatment have forced scientists around the world to move quickly to develop a vaccine against this virus. As of January 12, 2022, a few vaccines obtained emergency use listing from the WHO.[8] Types of COVID-19 vaccines that have received distribution permits can be seen in Table 1.

Along with the continued increase in COVID-19 cases, the Indonesian Government issued a COVID-19 vaccination program to prevent further spread of the virus transmission. Based on the Decree of the Minister of Health No. HK.01.07/MENKES/9860/2020 regarding the determination of the type of COVID-19 vaccine to be used for the COVID-19 vaccination program in

Indonesia, namely the Merah Putih, AstraZeneca, Sinophram, Moderna, Pfizer, and Sinovac vaccines, the first vaccination was carried out on January 13, 2021, using the Sinovac vaccine.

Adverse events following immunization (AEFI) are medical events related to immunization in the form of side effects or vaccine effects, toxicity, sensitivity reactions, pharmacological effects or program errors, coincidences, injection reactions, or anxiety and does not always have a causal relationship with the vaccine used.[9] Previous research on AstraZeneca AEFI of 1503 health workers at a hospital in Korea, during March 2021, showed that the most commonly reported AEFI were pain at the injection site (94.5%), fatigue (92.9%), injections (88.0%), and malaise (83.8%). The severity of most AEFI was mild to moderate, and the number of AEFI was lower in older age groups. There are no serious events requiring hospitalization, and most AEFIs improve within a few days.[10] The purpose of this study is to identify AEFI that occurred in Sinovac vaccine recipients at the Wirasakti Hospital Kupang.

Materials and Methods

Study design

This is a cohort study with a quantitative approach that aims to determine the incidence of AEFI in recipients of the first dose of the Sinovac vaccine. The method used is the observation method with a direct assessment of the subject followed prospectively longitudinally until a certain time.[11] The population in this study was 198 people who were recipients of the Sinovac vaccine at the Wirasakti Hospital, Kupang. 51 people were randomly selected as respondents in the study by using statistical calculations. The criteria for vaccine recipients and instructions for recording AEFI refer to the technical guidelines issued by the Ministry of Health, namely the Decree of the Director General of Disease Prevention and Control Number HK.02.02/4/1/2021. Evaluation is carried out within 30 minutes after the vaccine injection is carried out.

Ethical considerations

The ethical review in this research was issued by the Ethics Commission of the Faculty of Medicine University of Nusa Cendana with study approval number 36/UN15.16/KEPK/2021 (Registration No. UN02210436). Written informed consent was obtained from the participants. To protect data, researchers used a form issued by the health authority institution, and each data was coded by a series of numbers to protect the confidentiality of participants.

Results

An evaluation conducted 30 minutes after the respondent received the vaccine showed that the most common clinical manifestations were palpitations in 14 of 15 respondents (93%), dizziness in 13 respondents (87%), shortness of breath in 12 respondents (80%), and cramping and shaking in each hand in 1 respondent (7%). The total number of participants who experienced AEFI were women. Each participant experienced at least two clinical manifestations of AEFI. Details of these clinical manifestations can be seen in Table 2. Table 3 shows that most of the participants who experienced dizziness, palpitations, and shortness of breath were 11 people (73.33%), while the other AEFIs only occurred in 1 person (6.67%). Clinical manifestations of AEFI based on the age range of the respondents are shown in Table 4.

Discussion

All AEFI manifestations that occur are non-serious AEFIs, in the form of feeling dizzy, heart fluttering, shortness of breath, and cramps. Serious AEFI is any medical event after immunization that causes hospitalization, disability, and death and causes unrest in the community. Based on this understanding, all clinical manifestations that occur in respondents in this study are considered non-serious AEFI.

The AEFI manifestation that occurs is different from the results of the Sinovac vaccine stages 1 and 2, where the AEFI that occurs is pain at the injection site. The Sinovac vaccine AEFI report in Hong Kong contained 61 non-serious AEFI cases, 45 of which required hospital treatment. A serious AEFI that caused death also occurred in a 71-year-old man; the cause of his death is still being investigated. There were also 2 other deaths but they were not vaccine-related. In the Philippines, of the 892 Sinovac vaccine recipients, 872 had non-serious AEFIs and 20 had serious

Table 1. Types of COVID-19 vaccine.

Vaccine name	Supply country	Permit date
BNT162b1/BNT162b2 or Pfizer	Germany and USA	31 December 2020
The SII/COVISHIELD and AstraZeneca /AZD1222 vaccines	England	16 February 2021
The Janssen/Ad26.COV 2.S vaccine	Netherlands	12 March 2021
mRNA-1273 or moderna vaccine	USA	30 April 2021
The Sinopharm COVID-19 vaccine	China	7 May 2021
The Sinovac-CoronaVac vaccine	China	1 June 2021

Table 2. Clinical manifestation of adverse events following immunization after Sinovac vaccination.

AEFI	N	Percentage (%)
Dizziness	13	87
Tachycardia	14	93
dyspnea	12	80
Cram on hand	1	7
Hands shaking	1	7

AEFI, adverse events following immunization; n, number.

AEFIs. A health worker died a few days after receiving the Sinovac vaccine, the cause of which is still being investigated.[12]

The results of this study indicate that AEFI occurred in 15 people above all occurred in women. One of the most basic things that causes the diversity of immune responses induced by vaccination is gender;[13] however, the mechanism that occurs in it is still not systematically explained and this difference may be caused by vaccines that have been used and the immune response.

The results of the vaccine adverse event reporting system report from 2000-2006 indicate that the majority of AEFI occur in adult women (61%) and appear within 1-2 days after vaccination, the results of the AEFI report in Ontario also show that women are 7 times more likely to experience AEFI compared to men.[13,14] These study results also showed the same results where all of the 15 vaccine participants who experienced AEFI were women. The majority of AEFI that occur are non-serious because the majority of them only last for 1 day.

Women are more likely to experience AEFI such as fever, pain, and inflammation after the vaccine.[13,15,16] The biological process that distinguishes the vaccine response between men and women involves many factors; although the main cause is not known with certainty, it is suspected that immunity, hormonal, genetic, and microbial factors play a role.[14]

Passive reports of local reactions (such as pain, dizziness, redness, and inflammation) are more common in women.[15] Measurements of localized erythema and induration associated with inflammation showed that both younger and older women had larger sizes than men.[17]

The hypothesis that has been put forward regarding the differences in immunity between men and women is that steroid hormones, especially testosterone, estradiol, and progesterone, affect immune cell function.[18] Differences in the immune hormonal system due to sex were observed early in puberty, during the period of reproductive development, suggesting that sex hormones are not the only cause of different responses of the immune system to vaccines.[13,19] Another influencing factor is genetics, which causes differences in response to vaccines. Some of the differences may be due to hereditary factors caused by imbalances in the expression of genes encoded in the X and Y chromosomes. Some immune system-related genes and microRNA regulation are encoded in the X chromosome and there is some evidence that the activation of these genes is greater in females than in males.[20,21] Differences in sex chromosomes and autosomal genes encoding immune proteins may also contribute to differences in immune and antibody responses to vaccines.[22]

When exposed to pathogenic infection, men and women experience very different immune responses. Women generally have stronger immune systems than men.[23] Many clinical studies of vaccines show differences in immunity between men and women. Immunity ability in women is greater than in men due to the production of antibodies by B cells. In particular, the ability to produce more antibodies to protect themselves, and the effect of the vaccine to produce antibodies tends to be better in women,[24,25] but women also experience AEFI more frequently.[26-28] This is considered to be one of the reasons why women experience AEFI more frequently than men, as women have a stronger immune system than men, which causes a stronger response and increases side effects in the form of AEFI.

The results of AEFI reporting (passive reporting) on influenza vaccines show that women experience AEFI more often than men in all age groups.[15] The results of measuring local reactions associated with inflammatory reactions show that they are greater in women than in men.[14] The results of this study also show that AEFI occur are more common in the form of dizziness, palpitations, and shortness of breath.

The results of AEFI reporting in Canada for all types of COVID-19 vaccines used (Pfizer, Moderna, and AstraZeneca) show the same results, namely that AEFI is more common in women.[29] Although the results of this study indicate a relationship between gender and AEFI, the current global reporting of AEFIs is generally passive, meaning that no AEFI is waiting for reports from the public, and in general this shows that women are more likely to report AEFI than men. It also shows that more women received the vaccine: in this study, more women were vaccinated than men. Since one vaccine dose or administration schedule may differ between men and women, scientific evidence of sex-based vaccine response needs to be increased through clinical trials.[30]

Table 3. Adverse events following immunization in Sinovac vaccine participants.

AEFI	N	Percentage (%)
Dizziness, palpitations, shortness of breath	11	73.33
Dizziness and heart palpitations	1	6.67
Heart pounding and hands shaking	1	6.67
Dizziness, pain in the hands.	1	6.67
Shortness of breath and heart palpitations	1	6.67
Total	15	100

AEFI, adverse events following immunization; n, number.

Table 4. Clinical manifestations of adverse events following immunization based on the age range of respondents.

Age range	Experiencing AEFI				Total	
	Yes	%	No	%	n	%
18-30	9	17.6	16	31.4	25	49.0
31-45	6	11.8	12	23.5	18	35.3
46-59	0	0	8	15.7	8	15.7
Total	15	29.4	36	70.6	51	100

AEFI, adverse events following immunization.

Conclusions

The results of this study indicate that the Sinovac vaccine is relatively safe to use because only a small proportion of respondents (29.4%) experienced AEFI. The AEFI experienced by respondents is still in the non-serious category. Participants who experienced AEFI in this study were all women. This result is quite important because it can be the basis for knowing why and how the immune system of men and women react to vaccines so that it can be used as a reference for the use of vaccines in the future.

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