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Brief Communication

Survey of Adverse Events After The First Dose of The ChAdOx1 nCoV-19 Vaccine: A Single-Center Experience in Korea

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No conflicts of interest.

ABSTRACT

Vaccination is an important strategy for controlling the coronavirus disease 2019 (COVID-19) pandemic. We conducted a web-based cross-sectional survey based on Google Forms to collect data on adverse events (AEs) after the first dose of the ChAdOx1 nCoV-19 vaccine for healthcare workers (HCWs). Among the 1,676 vaccinated HCWs, 59.5% (998/1,676) responded to the survey. In total, 809 (81.1%) respondents reported experiencing AEs. There were no serious AEs, such as anaphylaxis. The most common AE was pain at the injection site (76.2%), followed by fatigue (75.9%), myalgia (74.9%), and fever (58.4%). HCWs in the younger age group experienced significantly more AEs than in the older age group.

Keywords: Coronavirus disease; Vaccine; Adverse event; Surveillance

Since it was first reported in December 2019, coronavirus disease 2019 (COVID-19) has caused approximately 100 million cases and 2.7 million deaths to date [1]. Vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an important strategy to control the COVID-19 pandemic. Vaccines are being developed using various platforms, and vaccination has commenced [2]. The potential vaccines for COVID-19 include inactivated/weakened virus vaccines, protein-based vaccines, viral vector vaccines, RNA vaccines, and DNA vaccines [3]. As of April 2021, the COVID-19 vaccines available in the Korea are the ChAdOx1 nCoV-19 vaccine (Oxford/AstraZeneca, Cambridge, UK) and BNT162b2 vaccine (Pfizer/bioNTech, New York, NY, USA and Mainz, Germany) [4]. In Korea, starting on February 26, 2021, vaccination began for healthcare workers (HCWs).

There are various data on potential adverse events (AEs) following COVID-19 vaccination, but detailed reports on individual AEs after vaccination are limited. This real-world study aimed to identify AEs after COVID-19 vaccination.

This study was conducted in a 642-bed university-affiliated acute care hospital. COVID-19 vaccination for HCWs was conducted from March 8 to 12, 2021. HCWs between the ages of 20 and 64 years received their first dose of the ChAdOx1 nCoV-19 vaccine. The web-based cross-sectional survey was conducted from March 17 to 21, 2021 using Google Forms by sending the link of the survey via text message to mobile phones on March 17, 2021 to collect data on AEs after vaccination. Participation in the survey was voluntary and anonymous. This

Author Contributions

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study was approved by the institutional review board of Inje University Ilsan Paik Hospital (IRB number: ISPAIK 2021-03-030), with a waiver of consent. Data on basic information such as age, sex, height, and weight as well as local AEs (pain at the injection site, redness, and swelling) and systemic AEs (fever, chills, myalgia, headache, arthralgia, nausea, vomiting, diarrhea, dizziness, and fatigue) after vaccination were collected. For fever, the onset, duration, body temperature, and use of antipyretics after vaccination were investigated. In the case of myalgia, headache, arthralgia, and pain at the injection site, the degree of pain was investigated using the numeric rating scale (NRS), which is an 11-point scale for the self-reporting of pain. NRS scores of 1 - 5, 6 - 7, and 8 - 10 indicated mild, moderate, and severe pain, respectively [5]. The survey also contained questions about the duration of the longest lasting symptom after vaccination, regardless of the type of AE, and whether the HCWs had visited the outpatient clinic or emergency department due to AEs.

SPSS version 25 for Windows (IBM Corporation, Armonk, NY, USA) was used for all statistical analyses. Categorical variables were analyzed using the Chi-square test or Fisher's exact test, as appropriate. Continuous variables were analyzed using an independent sample *t*-test or the Mann–Whitney *U* test. A two-tailed *P*-value of <0.05 was considered significant.

Of the 1,925 HCWs, 1,676 (87.1%) were vaccinated against COVID-19. A total of 998 (59.5%, 998/1676) vaccinated HCWs responded during the survey period. There was a higher proportion of women than that of men (779 [78.1%] *vs.* 219 [21.9%]). Among the respondents, the most dominant age group was the 20 - 29 years age group (38.1% [380/998]) (**Table 1**). The distribution of age groups between the total vaccinated HCWs and survey respondents was similar.

Of the 998 respondents, 809 (81.1%) reported experiencing AEs. There were no serious AEs, such as anaphylaxis. The occurrence of AEs after vaccination was significantly related to age (**Table 1**). The rates of AEs by age group were as follows: 87.6%, 20 - 29 years age group; 82.4%, 30 - 39 age group; 83.2%, 40 - 49 years age group; 68.9%, 50 - 59 years age group; and 54.1%, 60 - 64 years age group (P <0.001). AEs were more common in women (83.7%) than in men (71.7%) (P <0.001). The most common AEs were local symptoms, including pain at the injection site (76.2%, 760/998), followed by systemic symptoms, such as fatigue (75.9%, 757/998), myalgia (74.9%, 748/998), fever (58.4%, 583/998), headache (57.4%, 573/998), dizziness (44.7%, 446/998), nausea (28.9%, 288/998), and diarrhea (12.9%, 129/998) (**Fig. 1**; **Table 2**). Among the 998 respondents, pain at the injection site (P <0.001), injection site swelling (P <0.001), injection site redness (P = 0.010), fatigue (P <0.001), myalgia (P <0.001), chills (P <0.001), fever (P <0.001), headache (P <0.001), dizziness (P <0.001), arthralgia (P = 0.001), and nausea (P <0.001) were more commonly reported in younger age groups (**Table 2**).

The characteristics of fever were analyzed in 583 respondents who reported having fever. Fever occurred within 12 h of injection in 50.9% (297/583) respondents, between 12 and 24 h in 44.6% (260/583) respondents, and after 24 h in 4.5% (26/583) respondents. The duration of fever was 2

Table 1. Occurrence of adverse events in different age groups

Age group (years)	Vaccinated healthcare workers	Respondents	Occurrence of adverse events	*P*-value
20 - 29	645	380	333 (87.6)	<0.001
30 - 39	382	216	178 (82.4)	
40 - 49	330	185	154 (83.2)	
50 - 59	267	180	124 (68.9)	
60 - 64	52	37	20 (54.1)	
Total	1,676	998	809 (81.1)	

Data are expressed as numbers (%) of patients, unless otherwise indicated.

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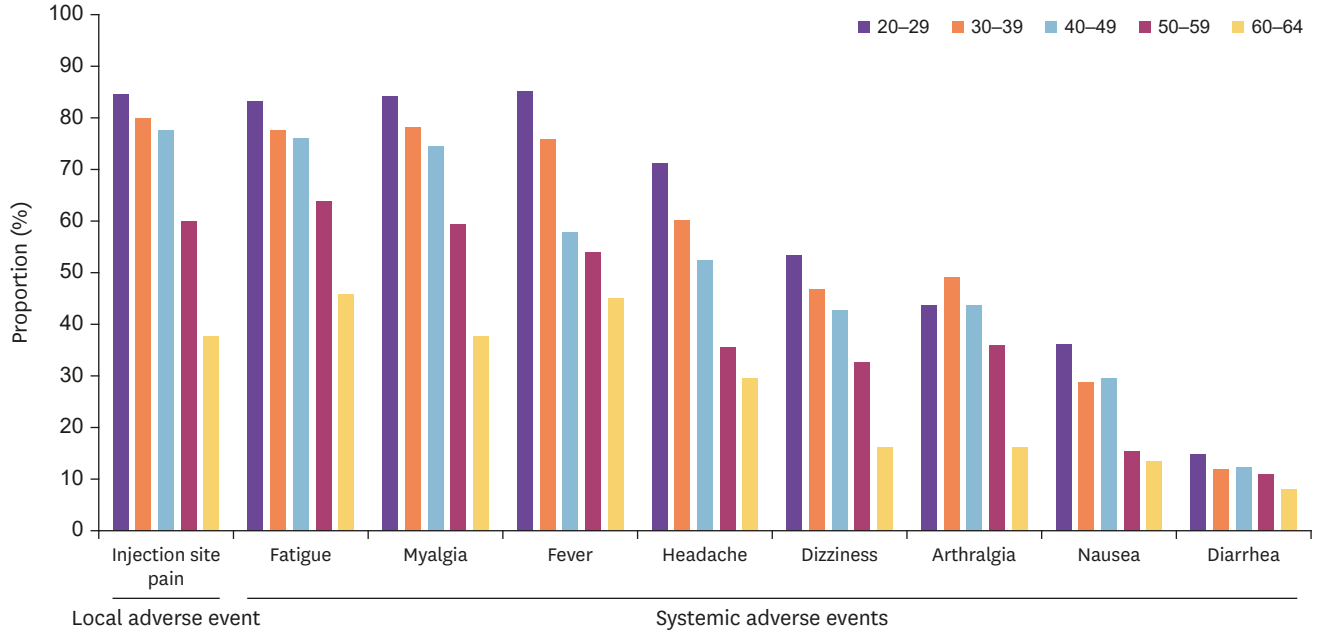

Figure 1. Frequency of common adverse events among 998 healthcare workers who responded to the survey by age groups.

Table 2. Frequency of adverse events among 998 respondents by age groups

Symptoms	Total (N = 998)	Age group (years)					*P*-value
		20 - 29 (N = 380)	30 - 39 (N = 216)	40 - 49 (N = 185)	50 - 59 (N = 180)	60 - 64 (N = 37)	
Local reaction							
Pain at the injection site	760 (76.2)	321 (84.5)	173 (80.1)	144 (77.8)	108 (60.0)	14 (37.8)	<0.001
Swelling	305 (30.6)	139 (36.6)	58 (26.9)	65 (35.1)	38 (21.1)	5 (13.5)	<0.001
Redness	163 (16.3)	79 (20.8)	31 (14.4)	32 (17.3)	17 (9.4)	4 (10.8)	0.010
Fatigue	757 (75.9)	316 (83.2)	168 (77.8)	141 (76.2)	115 (63.9)	17 (45.9)	<0.001
Myalgia	748 (74.9)	320 (84.2)	169 (78.2)	138 (74.6)	107 (59.4)	14 (37.8)	<0.001
Chills	608 (60.9)	274 (72.1)	139 (64.4)	111 (60.0)	75 (41.7)	9 (24.3)	<0.001
Fever	583 (58.4)	283 (74.5)	135 (62.5)	89 (48.1)	67 (37.2)	9 (24.3)	<0.001
Headache	573 (57.4)	271 (71.3)	130 (60.2)	97 (52.4)	64 (35.6)	11 (29.7)	<0.001
Dizziness	446 (44.7)	203 (53.4)	101 (46.8)	77 (42.8)	59 (32.8)	6 (16.2)	<0.001
Arthralgia	424 (42.5)	166 (43.7)	106 (49.1)	81 (43.8)	65 (36.1)	6 (16.2)	0.001
Nausea	288 (28.9)	138 (36.3)	62 (28.7)	55 (29.7)	28 (15.6)	5 (13.5)	<0.001
Diarrhea	129 (12.9)	57 (15.0)	26 (12.0)	23 (12.4)	20 (11.1)	3 (8.1)	0.571
Vomiting	28 (2.8)	14 (3.7)	5 (2.3)	3 (1.6)	4 (2.2)	2 (5.4)	0.498

Data are expressed as numbers (%) of patients, unless otherwise indicated.

days in 49.9% (291/583) respondents, 1 day in 38.6% (225/583) respondents, and >3 days in 11.5% (67/583) respondents. Among those who responded that they had experienced fever, 76.5% (431/583) actually measured their body temperature. Among those who had measured their body temperature, 26.4% (154/583), 24.4% (142/583), 18% (105/583), 7.2% (42/583) respondents had a temperature of <38.0°C, 38.0 - 38.4°C, 38.5 - 38.9°C, and 39.0 - 40.0°C, respectively. Moreover, 540 of the 583 (92.6%) respondents used antipyretics such as acetaminophen.

Body mass index (BMI) was calculated using the collected data on height and weight. From the data of 986 respondents who provided height and weight measurements, the following BMI (kg/m^2) distribution was noted: 72.5% (715/986), normal weight (18.5 ≤ BMI <25); 19.7% (194/986), overweight (BMI ≥25); and 7.8% (77/986), below normal weight (BMI <18.5). The lower the BMI, the more frequent were the AEs (P = 0.025) - below normal weight, 90.9% (70/77); normal weight, 81.3% (581/715); overweight, 77.8% (151/194).

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The median duration of the longest lasting symptoms after vaccination regardless of the type of AE was 2 days (interquartile range [IQR], 2 - 3 days). The duration of symptoms was 1 day in 15.3% (124/809) respondents, 2 days in 36.8% (298/809) respondents, 3 days in 24.5% (198/809) respondents, 4 days in 10.3% (83/809) respondents, and >5 days in 13.1% (106/809) respondents. Pain at the injection site, a local AEs, was categorized into mild (40.1%, 305/760), moderate (29.7%, 226/760), and severe (30.1%, 229/760). Systemic AEs such as myalgia, headache, and arthralgia were recorded as follows: mild, 30.3% (227/748), 29.3% (168/573), and 32.8% (139/424); moderate, 34.4% (257/748), 37.9% (217/573), and 35.6% (151/424); and severe, 35.3% (264/748), 32.8% (188/573), and 31.6% (134/424), respectively. Of the 809 respondents, 30 (3.7%) visited the outpatient clinic and 14 (1.7%) visited the emergency department because of AEs.

In this study, all HCWs received the ChAdOx1 nCoV-19 vaccine. The ChAdOx1 nCoV-19 vaccine was developed by Oxford University in the United Kingdom. It is developed with a replication-deficient chimpanzee adenoviral vector ChAdOx1 and contains the SARS-CoV-2 structural surface glycoprotein antigen (spike protein nCoV-19) gene [1, 6]. According to a previous phase 2/3 ChAdOx1 nCoV-1 vaccine clinical trial, pain at the injection site (41.4%, 53/128) and tenderness (63.3%, 81/128) were the most common local AEs in the standard-dose-vaccinated group [2], as in our study. The reactogenicity was lower and the vaccine was more tolerable in older adults than in younger adults, with similar immunogenicity across age groups after a booster dose [2].

The strength of this study is that it used large-scale data (998 respondents, corresponding to 58.8% vaccinated HCWs) and that it was possible to compare AEs across a range of adult ages. Among the respondents who reported experiencing AEs in this study, 94.6% respondents had self-limiting AEs that resolved without visiting an outpatient clinic or emergency department and were sufficiently controlled with acetaminophen. In a previous study, pain at the injection site and systemic pain were reported by fewer participants after prophylactic acetaminophen use [7]. The Korea Centers for Disease Control and Prevention has established a reporting system for COVID-19 vaccine-related AEs to monitor the occurrence of AEs after COVID-19 vaccination [8], but there is a possibility that minor symptoms may not be reported via this system. Although the relationship between BMI and AEs of COVID-19 vaccine is not clear, a recent study reported that humoral response was more efficient in the underweight and normal-weight groups than in the pre-obesity and obesity groups after the second dose of the BNT162b2 vaccine [9]. More research is needed on the relationship between BMI and AEs or vaccine efficacy. The results of this study are meaningful for predicting AEs that may occur when vaccinating the entire community.

Since AEs were not investigated prospectively and not all vaccinated HCWs participated, the accuracy of the data in this study may be limited. In addition, we cannot completely rule out the possibility that a single HCW may have responded to the questionnaire multiple times because of the anonymous survey. However, our results showed that a large number of vaccinated HCWs experienced AEs; thus, preparation to manage this issue is necessary. Furthermore, follow-up investigations after the second vaccination will also be meaningful.

After the first dose of the COVID-19 vaccine, a significant number of HCWs developed fever and pain at the injection site. AEs were more frequent in young HCWs. Therefore, before the second dose of COVID-19 vaccination, sufficient education and preparation are needed.

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