Issues on COVID-19 vaccines

Adverse events following COVID-19 vaccination in adolescents aged 16-17 years

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Abstract

In the Republic of Korea, the Pfizer-BioNTech COVID-19 mRNA vaccine was administered to adolescents aged 16-17 from July 19, 2021. To identify the adverse events (AEs) after vaccination, we have been monitoring AEs reported to the Korea Immunization Management System (KIMS) and the results of active monitoring of health conditions using text messages.

In this paper, we reviewed reports of AEs for adolescents aged 16-17 years who received the first dose of the Pfizer-BioNTech vaccine between October 18, 2021, and November 6, 2021 and monitored results of health conditions using text messages from day 0 to day 7 after vaccination.

A total of 1,525 AEs cases were reported via the KIMS from October 18, 2021, to November 6, 2021. The total reported rate of AEs was 0.29% compared to the number of doses administered. Among the total of AEs reported, the majority were non-serious (1,497 cases), such as headache, chest pain, dizziness, and myalgia. A total of 28 cases of serious AEs, including suspected anaphylaxis were reported. The mobile phone text messages monitoring received reports of health status from a total of 4,566 adolescents aged 16-17 years who received Pfizer-BioNTech vaccinations. 57.51% reported having health problems from day 0 to day 7 after vaccination. The types of health problems were injection site pain, myalgia, fatigue/tiredness, and headache.

This paper was a preliminary analysis of AEs after the first dose of the Pfizer-BioNTech for COVID-19 for adolescents aged 16-17 in the Republic of Korea. The KDCA will monitor AEs and implement the safe vaccination program by sharing and reviewing information with the committees and experts.

Keywords: COVID-19 vaccination, Adolescents aged 16-17 years, Adverse events

Introduction

Vaccination is the most effective tool to prevent the spread of coronavirus disease (COVID-19). The Pfizer-BioNTech COVID-19 mRNA vaccine was approved by the Ministry of Food and Drug Safety (MFDS) for vaccination on March 5, 2021, for persons aged 16 years and over [1]. On July 16, 2021, MFDS expanded its vaccination program to include adolescents aged 12-15 years, based on the evidence of its safety, immune response, and efficacy in adolescents aged 12-15 years [2]. Considering domestic infection risk and the epidemiological situation, the Pfizer-BioNTech COVID-19 mRNA vaccine was administered to third-year high school students and staff first from July 19, 2021, following the recommendations of the Korea Expert Committee on Immunization Practices (KECIP). Countries conducting COVID-19 vaccination recognize that unexpected adverse events (AEs) may occur after vaccination and evaluate the safety of COVID-19 vaccination via monitoring AEs after vaccination.

In the Republic of Korea, passive surveillance has been initiated, in which medical doctors and health care workers can report AEs to the Korea Immunization Management System (KIMS) to collect data on vaccine safety, identifying potential safety signals for further evaluation with reporting statistics of AEs periodically [4]. In addition, survey-based active surveillance using phone text messages has been implemented to monitor the health status for seven days after vaccination in a specific population group. This article summarized the results of passive surveillance by monitoring and analyzing the AEs reported to the KIMS and the effects of active surveillance of health conditions using text messages after the first dose of the COVID-19 vaccine for adolescents aged 16-17 years in the Republic of Korea.

Methods

1) Reports of AEs via the KIMS for COVID-19

AEs after the first vaccination against COVID-19 in adolescents aged 16-17 years were reported to the KIMS by medical institutions according to the 'Infectious Disease Control and Prevention Act' and the COVID-19 Vaccination Adverse Events Management Guidelines. As COVID-19 vaccines have been rolled out for adolescents aged 16-17 years since October 18, 2021, this study reviewed reports of AEs for adolescents aged 16-17 years (adolescents who were born between 2004-2005) who received the first dose of Pfizer-BioNTech vaccine from October 18, 2021, to November 6, 2021. Symptoms reported in this study are assessed based on the data reported to the KIMS for COVID-19 by different medical institutions and do not indicate accurate diagnosis and causality. Thus, caution needs to be exercised in interpreting the results.

2) Monitoring of health status using mobile phone text messages

The health status of adolescents aged 16-17 years who received the vaccine on/after October 18, 2021, and adolescents with smartphones who agreed to receive text messages was monitored daily through text messages for 7 days after the first vaccination for any AEs.

Text messages were forwarded to adolescents every day, and the respondents answered questions regarding their health status by accessing the website guided in the text message. A system was established in advance to store the participants' responses in the KIMS. The questionnaire consisted of items on general health status, symptoms at the injection site, systemic reactions, the ability to perform normal daily activities, and the use of medical care or type of medical institution visited due to AEs. A questionnaire tool transformed into easy-to-understand language was developed and conducted to minimize the response bias. Adolescents aged 16-17 years (born between 2004-2005) who received the first dose of Pfizer-BioNTech vaccine from October 18, 2021, were included for the analysis.

Results

1) Analysis results of reported AEs for adolescents aged 16-17 years

From October 18, 2021, to November 6, 2021, a total of 519,005 Pfizer-BioNTech vaccinations were provided to adolescents aged 16-17 years (first dose). By November 6, 2021, 1,525 cases of AEs were reported. The total reported rate of AEs was 0.29% compared to the number of doses administered. Since each individual could report multiple AEs, duplicate AEs reported were not removed in the results. The reported rate of

AEs was 0.31% (793 cases) in female, which was higher than 0.28% (732 cases) in male. By age, the reported rate of AEs was 0.30% (858 cases) among adolescents 17 years of age, which was higher than 0.29% (667 cases) for adolescents 16 years of age.

Among the total AEs reported, 1,497 were non-serious, such as headache, chest pain, dizziness, and myalgia. A total of 28 serious AEs, including suspected anaphylaxis were reported, and there were no deaths. Among the serious AEs, there were a total of 17 cases of others, including Adverse Events of Special Interest (AESIs) (Table 1).

Among the 1,497 reports of non-serious AEs, the headache was the most common symptom at 27.52% (412 cases), followed by chest pain at 23.31% (349 cases), dizziness at 15.43% (231 cases), myalgia at 15.36% (230 cases), and vomiting at 13.83% (207 cases). Among the serious AEs, anaphylaxis was the most common symptom at 39.29% (11 cases), followed by convulsions/seizures at 17.86% (5 cases) and acute paralysis at 14.29% (4 cases). A total of 31 cases required hospitalization. There were no reported cases of myocarditis and pericarditis, which are known expected AEs after Pfizer-BioNTech vaccinations for adolescents. There was one case of acute cardiovascular injury (Table 2).

2) Analysis results of monitoring of health status using mobile phone text messages for adolescents aged 16-17 years

The mobile phone text messages monitoring received reports of health status on day 0 from a total of 4,565 adolescents aged 16-17 years who received Pfizer-BioNTech vaccinations (October 18, 2021-Oct 27, 2021). A single respondent reported multiple AEs from day 0 to day 7 duplicated, thus, duplicate responses were removed based on the respondent. The rate of responses was 48.34% in males (2,207 persons) and 51.66% in females (2,359 persons). By age, the response rate among adolescents aged 17 years was higher (73.61%, 3,361 persons) than the response rate among adolescents 16 years of age (26.39%, 1,205 persons). On day 7 after vaccination, a total of 519 adolescents reported their health status using mobile phone text messages. The response rate was 52.02% in males (270 persons) and 47.98% in females (249 persons). By age, the rate of response was 45.09% (234 persons) in adolescents aged 16 years and 54.91% (285 persons) in adolescents aged 17 years respectively (Table 3).

Among 2,626 (57.51%) respondents who reported having health problems at least once throughout the follow-up period (day

Table 1. Adverse events (AEs) reports for adolescents aged 16–17 years who received the first dose of the Pfizer–BioNTech COVID–19 vaccine (October 18, 2021–November 6, 2021)

Category		Number of doses administered	Number of AEs (case)	Rate of AEs (%)	Non-serious AEs (case)	Serious AEs (case)			
						Subtotal	Death	Anaphylaxis suspected	Others[b]
Total		519,005	1,525	**0.29**	1,497	28	0	11	17
Sex	Male	261,166	732	**0.28**	718	14	0	6	8
	Female	257,839	793	**0.31**	779	14	0	5	9
Age	16 years	232,068	667	**0.29**	654	13	0	6	7
	17 years	286,937	858	**0.30**	843	15	0	5	10

[a] Adolescents (16–17 years): Those who were born between 2004–2005.
[b] Others: Adverse Events of Special Interest (AESIs), ICU admission, life–threatening, persistent significant disability or incapacity
※ This data were analyzed based on reports obtained from the Korea Immunization Management System (KIMS) for COVID–19 (http://is.kdca.go.kr) and do not imply accurate diagnosis or causality with the vaccine.

Table 2. Symptoms of adverse events (AEs) and hospital treatment for adolescents aged 16–17 years after the first dose of the Pfizer–BioNTech COVID–19 vaccine (October 18, 2021–November 6, 2021)

Symptoms of AEs and hospital treatment	Reporting cases	Reporting %
Non-serious AEs	1,497	
Headache	412	27.52
Chest pain	349	23.31
Dizziness	231	15.43
Myalgia	230	15.36
Nausea	207	13.83
Abdominal pain	80	5.34
Chills	78	5.21
Vomiting	78	5.21
Allergy reactions	71	4.74
Fever	66	4.41
Diarrhea	59	3.94
Pain, redness or swelling at the injection site within 3 days after vaccination	58	3.87
Abnormal uterine bleeding (AUB)	18	1.20
Lymphadenitis	12	0.80
Cellulitis (inflammation rather than abscess at the injection site)	7	0.47
Arthritis	6	0.40
Severe local adverse events	6	0.40
Thrombocytopenic purpura	2	0.13
Abscess at the injection site	1	0.07
Serious AEs	28	
Anaphylaxis (including anaphylactoid reactions)	11	39.29
Convulsions or seizures	5	17.86
Acute paralysis	4	14.29
Vaccine-associated enhanced disease (VAED)	2	7.14
Encephalopathy or encephalitis	1	3.57
Thrombocytopenia	1	3.57
Acute cardiovascular injury (excluding myocarditis and pericarditis)	1	3.57
Acute respiratory distress syndrome (ARDS)	1	3.57
Hospitalization	31	–

[a] Adolescents (16–17 years): Those who were born between 2004–2005.
※ This data were analyzed based on reports obtained from the Korea Immunization Management System (KIMS) for COVID–19 (http://is.kdca.go.kr) and do not imply accurate diagnosis or causality with the vaccine.

0-7) after the first dose of Pfizer-BioNTech COVID-19 vaccine, 2,313 (50.66%) adolescents reported local reactions at the injection site, and 2,300 persons (50.37%) adolescents reported systemic reactions. The most frequently reported reaction/health problem among adolescents aged 16-17 years after dose 1 was injection site pain at 46.32% (2,115 cases), followed by myalgia at 34.06% (1,555 cases), fatigue/tiredness at 28.82% (1,316 cases), headache at 22.40% (1,023 cases), swelling at 11.13% (508 cases) and chills at 9.79% (447 cases). 14.70% of respondents (671 persons) reported that they were not able to perform normal

Table 3. Number of respondents for the mobile phone text monitoring for adolescents aged 16–17 years who received the first dose of the Pfizer–BioNTech COVID–19 vaccine (Days 0–7, October 18, 2021–November 4, 2021)

Category		Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Total (%)		4,566 (100)	2,713 (59.42)	2,135 (46.76)	1,399 (30.64)	1,242 (27.20)	1,066 (23.35)	932 (20.41)	519 (11.37)
Sex (%)	Male	2,207 (48.34)	1,318 (48.58)	1,042 (48.81)	687 (49.11)	615 (49.52)	539 (50.56)	479 (51.39)	270 (52.02)
	Female	2,359 (51.66)	1,395 (51.42)	1,093 (51.19)	712 (50.89)	627 (50.48)	527 (49.44)	453 (48.61)	249 (47.98)
Age (%)	16 years	1,205 (26.39)	723 (26.65)	572 (26.79)	373 (26.66)	349 (28.10)	309 (28.99)	268 (28.76)	234 (45.09)
	17 years	3,361 (73.61)	1,990 (73.35)	1,563 (73.21)	1,026 (73.34)	893 (71.90)	757 (71.01)	664 (71.24)	285 (54.91)

daily activities. 1.91% of respondents (87 persons) required a visit to a medical facility. Seventy-seven adolescents (1.96%) went to a clinic, and 11 adolescents (0.24%) visited emergency rooms. Three adolescents (0.07%) were hospitalized. The overall reported rate of reactions/health problems was greater on day 0 after receiving a vaccination (54.40%, 1,476 persons) and gradually decreased over time. On day 7 after vaccination, it was the lowest at 6.36% (33 cases) (Table 4).

Conclusion

In the United States (U.S.), the most reported AEs after the first dose of the Pfizer-BioNTech vaccinations for adolescents aged 12-17 years (December 14, 2020-July 16, 2021) were dizziness (21.2%), syncope (14.4%), nausea (10.4%), and headache (10.0%) [5]. In the Republic of Korea, headache (27.52%) was the most reported AE among adolescents aged 16-17 years. Reports of headaches were followed by chest pain, dizziness, myalgia, and nausea as non-serious AEs, which differed from the U.S. However, as this result did not include adolescents aged 12-15 years, AEs after the first vaccination in adolescents aged 12 to 15 years should be identified to provide additional safety information by conducting a comprehensive analysis of AEs in adolescents aged 12-17 years.

The results of active surveillance after the first dose for adolescents aged 16-17 in the U.S. were 62.7% for local reactions at the injection site and 55.7% for systemic reactions, which were slightly higher than that of the Republic of Korea (local: 50.66%, systemic: 50.37%). The most reported local reactions in both the U.S. and the Republic of Korea were injection site pain, but there was a difference in their rates, accounting for 46.32% in the Republic of Korea and 60.2% in the U.S. In addition, as for systemic reactions, headache, myalgia, and fatigue were the most reported events in both countries, and myalgia was the most common in the Republic of Korea (34.06%), but fatigue (34.1%) was the most common in the U.S. [5].

This paper was a preliminary analysis of AEs after the first dose of the Pfizer-BioNTech for COVID-19 for adolescents aged 16-17 in the Republic of Korea. AEs reported included headaches, chest pain, dizziness, myalgia, and nausea. As a result of text message monitoring, pain at the injection site, myalgia, and fatigue/tiredness were reported. However, since the results were reported by self-reported questionnaires, the results may have been overestimated by parents or guardians of adolescents. Moreover, this result cannot be generalized to all adolescents in the Republic of Korea; thus, caution needs to be exercised in interpreting the results. The KDCA will monitor

Table 4. Reactions and health status reported to the mobile phone text monitoring for adolescents aged 16–17 years after the first dose of the Pfizer–BioNTech COVID–19 vaccine (Day 0–7, October 18, 2021–November 4, 2021)

Category	Post-vaccination (day)								
	Days 0–7[a]	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Health problems (%)	2,626 (57.51)	2,028 (44.42)	1,476 (54.40)	562 (26.32)	224 (16.01)	127 (10.23)	80 (7.50)	67 (7.19)	33 (6.36)
Fever or heat (%)	475 (10.40)	203 (4.45)	270 (9.95)	107 (5.01)	35 (2.50)	15 (1.21)	11 (1.03)	16 (1.72)	3 (0.58)
Local reactions (%)	2,313 (50.66)	1,701 (37.25)	1,341 (49.43)	445 (20.84)	148 (10.58)	68 (5.48)	39 (3.66)	29 (3.11)	8 (1.54)
Pain	2,115 (46.32)	1,546 (33.86)	1,230 (45.34)	402 (18.83)	114 (8.15)	45 (3.62)	24 (2.25)	17 (1.82)	4 (0.77)
Rash (redness)	95 (2.08)	31 (0.68)	44 (1.62)	20 (0.94)	8 (0.57)	3 (0.24)	2 (0.19)	2 (0.21)	0 (0.00)
Swelling	508 (11.13)	248 (5.43)	322 (11.87)	80 (3.75)	18 (1.29)	5 (0.40)	3 (0.28)	3 (0.32)	0 (0.00)
Itching	164 (3.59)	38 (0.83)	76 (2.80)	41 (1.92)	25 (1.79)	14 (1.13)	7 (0.66)	5 (0.54)	3 (0.58)
Urticaria	25 (0.55)	4 (0.09)	13 (0.48)	7 (0.33)	5 (0.36)	1 (0.08)	1 (0.09)	1 (0.11)	1 (0.19)
Others	271 (5.94)	140 (3.07)	94 (3.46)	27 (1.26)	14 (1.00)	15 (1.21)	12 (1.13)	7 (0.75)	2 (0.39)
Systemic reactions (%)	2,300 (50.37)	1,657 (36.29)	1,282 (47.25)	489 (22.90)	195 (13.94)	115 (9.26)	75 (7.04)	62 (6.65)	30 (5.78)
Chills	447 (9.79)	186 (4.07)	235 (8.66)	92 (4.31)	34 (2.43)	21 (1.69)	8 (0.75)	6 (0.64)	6 (1.16)
Headache	1,023 (22.40)	517 (11.32)	541 (19.94)	242 (11.33)	102 (7.29)	54 (4.35)	34 (3.19)	32 (3.43)	13 (2.50)
Joint pain	265 (5.80)	137 (3.00)	136 (5.01)	42 (1.97)	24 (1.72)	17 (1.37)	4 (0.38)	6 (0.64)	4 (0.77)
Myalgia	1,555 (34.06)	1,055 (23.11)	886 (32.66)	256 (11.99)	76 (5.43)	35 (2.82)	25 (2.35)	15 (1.61)	8 (1.54)
Fatigue or tiredness	1,316 (28.82)	823 (18.02)	672 (24.77)	264 (12.37)	103 (7.36)	68 (5.48)	37 (3.47)	35 (3.76)	15 (2.89)
Nausea	445 (9.75)	224 (4.91)	188 (6.93)	110 (5.15)	37 (2.64)	18 (1.45)	17 (1.59)	7 (0.75)	11 (2.12)
Vomiting	38 (0.83)	7 (0.15)	17 (0.63)	13 (0.61)	2 (0.14)	2 (0.16)	0 (0.00)	2 (0.21)	2 (0.39)
Diarrhea	177 (3.88)	48 (1.05)	86 (3.17)	52 (2.44)	17 (1.22)	10 (0.81)	8 (0.75)	8 (0.86)	5 (0.96)
Abdominal pain	239 (5.23)	80 (1.75)	128 (4.72)	58 (2.72)	26 (1.86)	15 (1.21)	10 (0.94)	6 (0.64)	7 (1.35)
Rash	12 (0.26)	6 (0.13)	6 (0.22)	2 (0.09)	0 (0.00)	0 (0.00)	1 (0.09)	0 (0.00)	0 (0.00)
Armpit tenderness	225 (4.93)	114 (2.50)	116 (4.28)	34 (1.59)	9 (0.64)	6 (0.48)	2 (0.19)	4 (0.43)	3 (0.58)
Others	222 (4.86)	79 (1.73)	85 (3.13)	42 (1.97)	23 (1.64)	24 (1.93)	17 (1.59)	16 (1.72)	9 (1.73)
Unable to perform normal daily activities (%)	671 (14.70)	280 (6.13)	390 (14.38)	152 (7.12)	60 (4.29)	51 (4.11)	30 (2.81)	22 (2.36)	16 (3.08)
Medical facilities visit (%)	87 (1.91)	8 (0.18)	16 (0.59)	25 (1.17)	20 (1.43)	13 (1.05)	10 (0.94)	10 (1.07)	8 (1.54)
Emergency department visit	11 (0.24)	1 (0.02)	3 (0.11)	3 (0.14)	4 (0.29)	2 (0.16)	1 (0.09)	1 (0.11)	0 (0.00)
Hospitalization	3 (0.07)	0 (0.00)	1 (0.04)	0 (0.00)	0 (0.00)	1 (0.08)	2 (0.19)	1 (0.11)	0 (0.00)
Clinic	77 (1.69)	7 (0.15)	12 (0.44)	22 (1.03)	16 (1.14)	10 (0.81)	7 (0.66)	8 (0.86)	8 (1.54)

[a] Response to phone text monitoring at least once during days 0–7 post-vaccination

※ Respondent can multiple report reactions/health problems on various days

AEs and implement the safe vaccination program by sharing and reviewing information with the committees and experts.

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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