SURVEY OF THE SHORT-TERM SAFETY OF THE VERO CELL COVID-19 VACCINE AMONG CHINESE CITIZENS IN LESOTHO

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Abstract. Emergency authorization was granted to administer a Vero Cell inactivated coronavirus disease-2019 (COVID-19) vaccine to Chinese citizens living in Lesotho from August 2021 to December 2021. We aimed to determine the safety of this vaccine in order to inform efforts to improve uptake of this vaccine. The inclusion criteria for study subjects were: being a Chinese citizen, willing to participate in this study, being aged ≥18 years, having no history of COVID-19 during the previous 6 months and having received 2 doses the study vaccine 28 days apart. Adverse reactions were assessed at 30 minutes and 7 days (by phone) after the first dose of the vaccine, and at 7, 30, 60, and 90 days after the second dose of the vaccine (by phone). A total of 1,289 subjects were included in the study, 828 (64.2%) males. 211 subjects (16.4%) reported an adverse reaction to the vaccine. Fatigue was the most common adverse reaction (n = 58, 4.5%), followed by pain at the injection site (n = 49, 3.8%), drowsiness (n = 34, 2.6%), dizziness (n = 23, 1.8%,) and headache (n = 15, 1.2%). The following adverse reactions were reported by <1.0% of subjects for each symptom: myalgia, diarrhea, fever, anorexia, arthralgia, induration of the injection site, erythema of the injection site, rash at the injection site, edema of the injection site, pruritis of the injection site and emesis. No severe adverse reactions were reported. In summary, the Vero cell-inactivated vaccine resulted in only mild adverse reactions among the Chinese study subjects in Lesotho. We conclude the vaccine is safe and Chinese in Lesotho should be educated about this safety profile in hopes of improving uptake of this vaccine in this patient population. Further studies are needed to determine if educating this population about this safety profile may improve the vaccine uptake.

Keywords: COVID-19, SARS-CoV-2, vaccine, vaccination, safety

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INTRODUCTION

In late 2019 coronavirus disease-2019 (COVID-19) (Chan *et al*, 2020; Chen *et al*, 2020; Li *et al*, 2020; Tan *et al*, 2020; Wang *et al*, 2020a; Zhu *et al*, 2020), caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), became an epidemic (Kaplan, 2020; Malande, 2020; Toulkeridis *et al*, 2020; Yang *et al*, 2020; Kwok *et al*, 2021) and then a pandemic (WHO, 2020b). By 10 March 2023, 676 million cases of COVID-19 with 6.8 million COVID-19 deaths had been reported worldwide (Johns Hopkins University, 2023).

Inactivated vaccines are widely used to prevent the emergence of infectious diseases (Stern, 2020). The relatively rapid development time of this type of vaccine makes it a promising strategy for COVID-19 vaccine development (Wang *et al*, 2020b). Two inactivated vaccine candidates were reported to protect non-human primates against SARS-CoV-2 with good safety in preclinical trials (Gao *et al*, 2020; Wang *et al*, 2020b). Xia *et al* (2021) reported the safety, tolerability and immunogenicity among health subjects in China of an inactivated vaccine candidate produced by Beijing Bio-Institute of Biological Products Co Ltd (BBIBP-CorV).

To protect Chinese citizens living overseas, the Chinese government launched the "Spring Seedling Campaign," to vaccinate Chinese citizens living in other countries with the COVID-19 vaccine; however, the safety of vaccination among Chinese citizens in Africa has rarely been reported. These safety data are important to inform efforts to control COVID-19 among Chinese nationals living in other countries.

In this study, we aimed to determine the safety of a Vero cell-inactivated COVID-19 vaccine produced by BBIBP-CorV (Wang *et al*, 2020b; WHO, 2020a), approved for emergency use by Chinese nationals in Lesotho, in order to reduce concerns about the safety of this inactivated COVID-19 vaccine

and to build confidence among the population regarding the vaccine.

MATERIALS AND METHODS

This study was conducted in the Kingdom of Lesotho, from August 2021 to December 2021 among Chinese citizens living in Lesotho who were vaccinated voluntarily. The inclusion criteria for study subjects were: being a Chinese citizen, willing to participate in this study, being aged ≥18 years, having no history of COVID-19 during the previous 6 months and having received 2 doses the study vaccine 28 days apart.

The following information was obtained from each subject: sex, age, weight, health status, and past medical history, COVID-19 vaccination history and dates and injection sites.

Adverse reactions were assessed at 30 minutes and 7 days (by phone) after the first dose of the vaccine, and at 7, 30, 60, and 90 days after the second dose of the vaccine (by phone). If a person had multiple adverse reactions, each reaction was considered as a separate episode. World Health Organization criteria were used to select adverse reaction symptoms (WHO, 2021).

The following were considered as vaccine adverse reactions: (1) Injection site reactions: pain, erythema, induration, tenderness or pruritis of the injection site; (2) Systemic reactions: fever, headache, dizziness, fatigue, drowsiness, anorexia, vomiting, diarrhea, myalgia, arthralgia, diffuse rash and diffuse pruritis.

All subjects gave written informed consent prior to inclusion in the study. Subjects were provided the vaccine whether they were willing to participate in the study or not. This study was approved by the Ethics Review Board of Medical Research, the 15th Batch of Assisting Lesotho Medical Team, Motebang Hospital Leribe (accession number: KY2021-01-01). The study was conducted in accordance with the Declaration of Helsinki.

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS), version 22 (IBM, Armonk, NY). After evaluating data normality and homoscedasticity, categorical variables were presented as percentages. Proportions were compared using the Pearson χ^2-test. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 1,289 subjects were included in the study; 828 (64.2%) males. The mean ± standard

deviation (SD) age of study subjects was 43 ± 11 (range: 18-76) years. All the subjects were Han Chinese (Table 1).

211 subjects (16.4%) experienced an adverse reaction to the COVID-19 vaccine (Table 2), 210 subjects (16.3%) with the first dose and 29 (2.3%) with the second dose (p<0.001) (Table 3). No serious vaccine-related adverse events were observed during this study.

The most common injection site adverse reaction was pain (n =49, 3.8%), followed by induration (n = 3, 0.2%), erythema (n = 3, 0.2%), rash (n = 2, 0.2%), edema (n = 1, 0.1%), and pruritis (n = 1, 0.1%).

Table 1

Demographic characteristics of the study subjects (N = 1,289)

Characteristic	Frequency* n (%)
Gender	
Male	828 (64.2)
Female	461 (35.8)
Age in years	
18-29	157 (12.2)
30-39	330 (25.6)
40-49	406 (31.5)
50-59	359 (27.8)
60-69	35 (2.7)
70-79	2 (0.2)
Age in years, Mean ± SD	43 ± 11
Weight in kilograms, Mean ± SD	65.9 ± 11.8
Nationality	
Han Chinese	1289 (100.0)

*Unless otherwise stated

SD: standard deviation

The most common systemic adverse reaction was fatigue (*n* = 58, 4.5%), followed by drowsiness (*n* = 34, 2.6%), dizziness (*n* = 23, 1.8%), headache (*n* = 15, 1.2%), myalgia (*n* = 10, 0.8%), diarrhea (*n* = 7, 0.5%),

Table 2

Incidences of adverse reactions among study subjects due to the COVID-19 vaccine after the first and second doses (N = 1,289)

Adverse reaction	First dose *n* (%)	Second dose *n* (%)	Either dose *n* (%)	*p*-value
Any adverse reactions	210 (16.3)	29 (2.3)	211 (16.4)	<0.001
Injection site adverse reactions				
Pain	49 (3.8)	11 (0.9)	49 (3.8)	<0.001
Induration	3 (0.2)	1 (0.9)	3 (0.2)	0.317
Redness	3 (0.2)	0 (0.0)	3 (0.2)	0.083
Rash	2 (0.2)	0 (0.0)	2 (0.2)	0.157
Swelling	1 (0.1)	0 (0.0)	1 (0.1)	0.317
Itching	1 (0.1)	0 (0.0)	1 (0.1)	0.317
Systemic adverse reactions				
Fatigue	57 (4.4)	14 (1.1)	58 (4.5)	<0.001
Sleeping	34 (2.6)	3 (0.2)	34 (2.6)	<0.001
Dizziness	23 (1.8)	1 (0.1)	23 (1.8)	0.000
Headache	15 (1.2)	2 (0.2)	15 (1.2)	0.002
Myalgia	10 (0.8)	1(0.1)	10 (0.8)	0.007
Diarrhea	7 (0.5)	0 (0.0)	7 (0.5)	0.008
Fever	5 (0.4)	1 (0.1)	5 (0.4)	0.102
Anorexia	4 (0.3)	1 (0.1)	4 (0.3)	0.179
Arthralgia	3 (0.2)	0 (0.0)	3 (0.2)	0.083
Vomiting	1 (0.1)	0 (0.0)	1 (0.1)	0.317

COVID-19: coronavirus disease 2019

Table 3

Incidences of adverse reactions to the COVID-19 vaccine among study subjects by time after vaccination (N = 1,289)

Adverse reaction	Within 1 week of the 1st dose *n* (%)	Within 1 week of the 2nd dose *n* (%)	30 days after the 2nd dose *n* (%)	60 days after the 2nd dose *n* (%)	90 days after the 2nd dose *n* (%)
Any adverse reactions	210 (16.3)	29 (2.3)	0 (0.0)	0 (0.0)	0 (0.0)

COVID-19: coronavirus disease 2019

fever (*n* = 5; 0.4%), anorexia, (*n* = 4, 0.3%), arthralgia (*n* = 3, 0.2%) and vomiting (*n* = 1, 0.1%) (Table 2).

DISCUSSION

Since the COVID-19 pandemic, there have been a number of COVID-19 vaccines produced (Cavaleri *et al*, 2021; US FDA, 2021) but post-introduction surveillance is necessary.

In our study, 16.4% of subjects experienced adverse reactions and no severe adverse reactions were reported. The adverse reactions were significantly more common with the first dose than the second dose of the vaccine with fatigue and injection site pain being the most common systemic and injection site reactions, respectively. During the Phases I and II of one of the Sinopharm COVID-19 vaccine trials (Xia *et al*, 2021), at least one adverse reaction was reported within 7 days of vaccination by 29% of subjects during Phase I and 23% of subjects during Phase II trials. In another Phase II Sinopharm COVID-19 vaccine trial, 19% of subjects reported an adverse reaction to the 3 μg dose of the vaccine and 18% with the 6 μg dose (Zhang *et al*, 2021). In a Phase III trial of the Sinopharm vaccine, most of the adverse events were mild to

moderate in severity, and consisted primarily of injection site reactions, headaches and fatigue (Al Kaabi *et al*, 2021; Al Kaabi *et al*, 2023).

In the Phase I and II trials of the Sinovac COVID-19 vaccine, one study reported 26% of subjects had an adverse reaction at a 1.5 μg dose, 29% at the 3 μg dose and 24% in the placebo group had an adverse reaction (p>0.05) (Han *et al*, 2021); with injection site pain being the most common injection site adverse reaction reported (16% with the 1.5 μg dose, 16% with the 3 μg dose and 2% in the placebo group; p<0.001) (Han *et al*, 2021). In the Phase III trials of the Sinovac vaccine, one study reported 18.9% of subjects had an adverse reaction while among those who received the placebo 16.9% reported an adverse (p=0.018), with the most common injection site adverse reaction being pain, followed by erythema, and the most common systemic adverse reactions being fatigue, headache and myalgia (Tanriover *et al*, 2021). In a randomized, placebo-controlled, observer-blinded trial of the Pfizer-BioNTech (BNT162b2) vaccine, the most common adverse reactions reported were fatigue, headache and transient mild to moderate injection site pain (Polack *et al*, 2020).

Limitation of our study were not all subjects may have reported adverse reactions and some may have had recall bias. The 4-month follow-up period in our study may have been short enough to determine adverse reactions and long enough to give a longer period of follow up; however, longer follow-up studies are needed to pick up the longer term effects of the vaccine.

In summary, the Vero cell-inactivated vaccine resulted in only mild adverse reactions among the Chinese study subjects in Lesotho. We conclude the vaccine is safe and Chinese in Lesotho should be educated about this safety profile in hopes of improving uptake of this vaccine in this patient population. Further studies are needed to determine if educating this population about this safety profile may improve the vaccine uptake.

ACKNOWLEDGEMENTS

This study was supported by the Embassy of the People's Republic of China in the Kingdom of Lesotho.

This work was financially supported by grants from Hubei Province Health and Family Planning Scientific Research Project (No. WJ2023M131) and from Wuhan

Municipal Health Commission Scientific Research Project (No. WX21Z73). Funding acquisition: Zhi Huang.

CONFLICTS OF INTEREST DISCLOSURE

The authors declare no conflicts of interest with respect to the research, authorship, and/or publication of this article.

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