Original Article

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Antibody Immune Response Compared between Recombinant Viral Vector and mRNA Vaccines among Health Care Personnel Who Had Previously Received 2 Doses of Inactivated COVID-19 Vaccine

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Abstract:

Background: Currently, a booster dose of AstraZeneca or Pfizer vaccine was introduced to healthcare personnel who had previously received two doses of inactivated vaccine.

Objective: To compare immune response and rate of adverse reactions after the third dose of AstraZeneca or Pfizer vaccines among healthcare personnel who had already received two doses of inactivated vaccine. We also determined immune response in those who received 2 doses of AstraZeneca vaccine.

Methods: We conducted an observational study at the Mae Fah Luang University Medical Center Hospital. We recruited healthcare personnel who had received AstraZeneca or Pfizer vaccine after 2 doses of Sinovac or received 2 doses of AstraZeneca vaccine. Those who were immunocompromised or had a history of COVID-19 infection were excluded. Participants were divided into 3 groups: (1) Sinovac-Sinovac-AstraZeneca, (2) Sinovac-Sinovac-Pfizer and (3) AstraZeneca-AstraZeneca. Immunoassay for anti-SARS-CoV-2 Spike protein (S) were performed at 30-60 days after the last vaccination dose. Adverse reactions after the third dose of vaccination were collected by using a questionnaire. We performed Kruskal Wallis test to compare antibody titer levels among the 3 groups. Comparisons of adverse reactions between group 1 and group 2 were analyzed using Chi-square or Fisher Exact test for categorical data as appropriate.

Results: There were 50, 111 and 18 participants of group 1, 2 and 3, respectively. All exhibited high titer levels of anti-SARS-CoV-2-S. The average antibody titer levels were highest in group 2 ($p < 0.001$), following by group 1 and group 3, respectively. Participants of group 1 reported fever and headache more frequently than those of group 2 ($p < 0.001$).

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Conclusion: Current vaccination regimens, booster AstraZeneca or Pfizer vaccine after two doses of inactivated vaccine and 2 doses of AstraZeneca are efficacious in producing immunity against SARS-CoV-2.

Keywords: COVID-19 vaccine, AstraZeneca, Pfizer, anti-SARS-CoV-2-S

Introduction

The coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has been declared an ongoing global pandemic since March 2020. In Thailand, the first case of COVID-19 was reported in January 2020. Since March 2020, the number of cases has continuously increased despite many control measures introduced by the government.[1] To date, the most effective way to control the COVID-19 pandemic is to administer vaccinations to most of the population.

In Thailand, the initial COVID-19 vaccine, CoronaVac (Sinovac) and ChAdOx1 nCoV-19 (AstraZeneca) were provided, starting in February-March 2021. However, due to problems of vaccine distribution and mutation of the coronavirus, the outbreak of the Delta strain continued with a rapidly increasing number of new cases and deaths.

In July 2021, The Ministry of Public Health issued a new guideline for vaccination to improve the efficacy of COVID-19 prevention and control.[2] Healthcare personnel who had received two doses of inactivated vaccine would be provided with a third dose of AstraZeneca or BNT162b2 (Pfizer) vaccine, at least 4 weeks after the second dose. Those who had received 2 doses of AstraZeneca were not applicable because immunity remained high for at least 6 months.

The Mae Fah Luang University Medical Center Hospital has provided the third dose of vaccine, AstraZeneca or Pfizer, to its personnel, according to the government guideline since July 2021. However, the efficacy of the third dose has not been reported. Therefore, we conducted a study to determine immune response and adverse reactions after the third dose compared between AstraZeneca and Pfizer vaccines among healthcare personnel who had previously received two doses of inactivated vaccine. In addition, we also determined the level of immunity in personnel who received two doses of the AstraZeneca vaccine.

Method

We conducted an observational study in healthcare personnel at the Mae Fah Luang University Medical Center Hospital. We recruited individuals aged more than 18 years old who received a third dose of AstraZeneca or Pfizer after 2 doses of CoronaVac (Sinovac) or received 2 doses of AstraZeneca. Those who were immuno-compromised or had a history of COVID-19 infection were excluded. Participants were divided into 3 groups, based on the type of vaccination: (1) Sinovac-Sinovac-Astra-Zeneca, (2) Sinovac-Sinovac-Pfizer and (3) AstraZeneca-AstraZeneca.

Participants were asked to answer a questionnaire including age, gender, weight, height, underlying diseases, date of COVID-19 vaccinations and adverse reactions within 7 days after the last dose.

Blood tests for antigen-specific humoral immune response were performed at 30-60 days after the last dose of COVID-19 vaccine, using a commercial immunoassay, Elecsys Anti-SARS-CoV-2 S assay (Roche Diagnostics).

The Elecsys Anti-SARS-CoV-2 S assay is an immunoassay used to detect antibodies

(including IgG) to the SARS-CoV-2 spike (S) protein receptor-binding domain (RBD). Quantification of the antibody response can measure the specific antibody titer, ranging from 0.4 U/mL to 250 U/mL (up to 2500 U/mL for 10-fold dilution, and up to 12,500 U/mL for 50-fold dilution).

As per the manufacturer's instructions, antibody titer 0.8 U/mL or higher was considered positive for anti-SARS-CoV-2 S. A result of 15 U/mL or higher had optimized correlation to surrogate virus neutralization method. A result of 132 U/mL or higher was considered as high titer for anti-SARS-CoV-2 S.[3]

The research protocol was approved by The Mae Fah Luang University Ethics Committee on Human Research (EC234/2021).

Statistical analysis

We performed Kruskal Wallis test to compare antibody titer levels among the 3 groups. Comparisons between group 1 and group 2 were analyzed using the Mann-Whitney U test for continuous data and Chi-square or Fisher Exact test for categorical data as appropriate. Factors associated with antibody titer levels and rate of adverse reactions between group 1 and 2 were analyzed using linear regression and logistic regression analysis, respectively. Statistically significant difference was considered at a p value of less than 0.05.

Result

There were 180 healthcare personnel who participated in the study. One case was excluded due to a 28-day interval between the 3rd dose and the time of the blood test. Fifty, 111 and 18 personnel were recruited to groups 1, 2 and 3, respectively. There were no differences in gender and underlying diseases among the groups. Regarding underlying diseases at risk, cardiovascular, chronic pulmonary and cerebrovascular diseases were reported in 1, 2 and 1 personnel of group 1, 2 and 3, respectively. Obesity was noted in 5, 3 and 2 personnel of group 1, 2 and 3, respectively. Participants of group 2 were younger than those of other groups. Body mass index (BMI) of group 1 was higher than that of group 2. All participants of group 1 and 2 received Sinovac vaccine for the first and second doses with no difference in the interval between doses. However, participants of group 2 received the third dose of vaccine significantly later than those of group 1. The interval between the last dose of vaccination and the time of blood test for immune response of group 2 was significantly longer than that of the other groups (Table 1).

All participants exhibited high titer levels of anti-SARS-CoV-2 S. The average antibody titer levels were highest in group 2, following by group 1 and group 3, respectively (Figure 1).

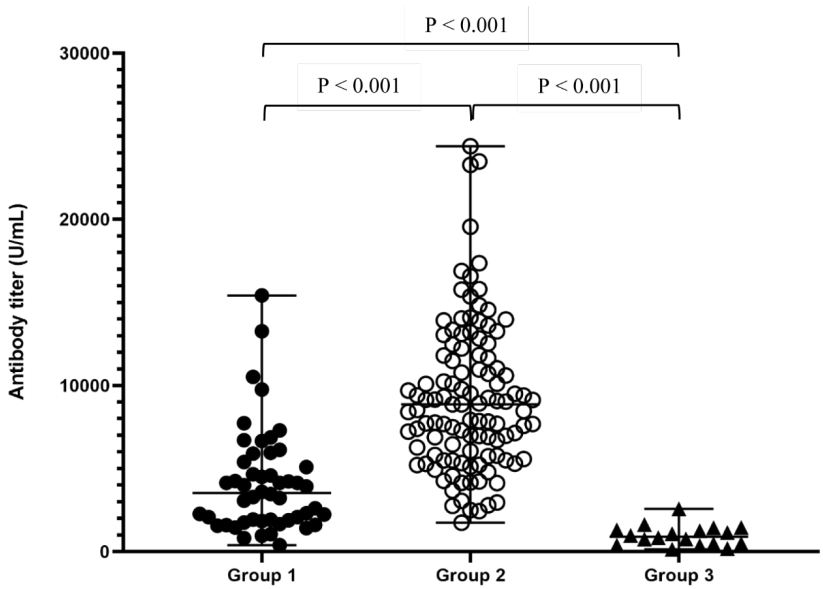
Besides the group, factors associated with antibody titer levels of group 1 and group 2 were the interval between the second and third doses of vaccination, the longer interval, and the higher antibody titer level (Table 2).

Overall adverse reactions reported after the 3rd dose of vaccination were not different between group 1 (78%) and group 2 (70.3%). However, participants of group 1 reported fever and headache more frequently than those of group 2 (Figure 2). Women reported symptoms nearly five-fold more frequently than men, related to adverse reactions after the 3rd dose of vaccination (Table 3).

Table 1 Demographic data of participants (N = 179)

Variables	Group 1	Group 2	Group 3	P value
n	50	111	18	
Male, n (%)	9 (18.0)	20 (18.0)	3 (16.7)	0.990
Age (year)	36.0 (21.0, 60.0)	31.0 (22.0, 57.0)	40.5 (21.0, 65.0)	0.001Ψ 0.436x 0.019δ
Body mass index (kg/m^2)	23.7 (17.9, 33.9)	21.6 (16.6, 33.2)	24.7 (18.7, 30.8)	0.026Ψ 0.739x 0.071δ
Underlying disease, n (%)	11 (22.0)	12 (10.8)	4 (22.2)	0.125
Interval (day) 1st - 2nd dose	21.0 (18.0, 26.0)	21.0 (21.0, 34.0)	84.0 (79.0, 102.0)	0.785Ψ
2nd - 3rd dose	63.0 (24.0, 103.0)	89.0 (13.0, 104)	NA	< 0.001Ψ
Last dose - blood test	53.0 (38.0, 56.0)	54.0 (52.0, 58.0)	52.0 (49.0, 58.0)	< 0.001Ψ 0.948x < 0.001δ

Ψ Comparison between group 1 and 2
x comparison between group 1 and 3
δ comparison between group 2 and 3



Median (U/mL)	3527.50	8859.00	903.00
Min (U/mL)	390.90	1740.00	134.10
Max (U/mL)	15425.00	24403.00	2574.00

Figure 1 Scatter plot of anti-SARS-CoV-2 S titer levels of 3 groups

Table 2 Factors associated to antibody titer compared between group 1 and group 2

Variables	Mean ± SD	Univariate		Multivariate	
		Standardized coefficient	P value	Standardized coefficient	P value
Group 2, n (%)	111 (68.9)	0.50 (3721.10, 6484.39)	<0.001	0.33 (1904.99, 4842.59)	<0.001
Male, n (%)	29 (18.0)	0.02 (-1685.22, 2157.92)	0.808	0.10 (-465.60, 2936.42)	0.153
Age (year),	33.39 ± 8.58	-0.24 (-214.13, -46.30)	0.003	-0.11 (-136.83, 11.27)	0.096
BMI (kg/m^2),	23.09 ± 3.88	-0.10 (-316.65, 63.30)	0.190	-0.002 (-169.95, 165.70)	0.980
Interval 2nd to 3rd dose (day)	75.29 ± 19.06	0.48 (83.56, 151.99)	<0.001	0.37 (57.18, 126.13)	<0.001

BMI: body mass index

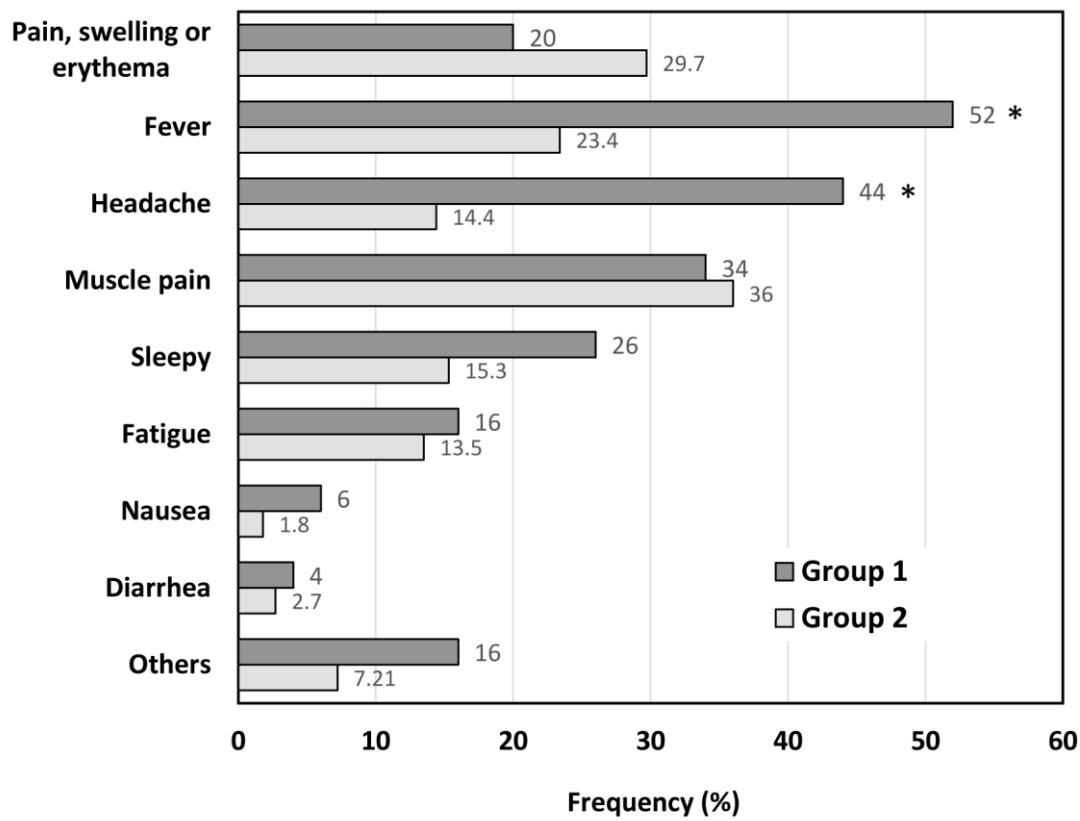


Figure 2 Comparison of adverse reaction rate (%) between group 1 and group 2
* $p < 0.001$

Table 3 Factors associated to adverse reaction after the 3rd dose of vaccination

Variables	N	Adverse reaction, n (%)	Odds ratio	95% CI	P value
Group 1	50	39 (78.0)	1.89	0.79, 4.50	0.153
Group 2	111	78 (70.3)	1		
Female	132	104 (78.8)	4.90	2.07, 11.62	< 0.001
Male	29	13 (44.8)	1		
Age (year), mean ± SD	33.39 ± 8.58	0.97	0.93, 1.01	0.155	

Discussion

To date, no study on the effect of a third boosting heterogenous vaccine after two doses of inactivated vaccine has been published. Corresponding to a previous study,[4] we demonstrated that boosting with either virus vectored (AstraZeneca) or mRNA (Pfizer) vaccine resulted in higher titer of anti-SARS-CoV-2 S in participants who had received two doses of inactivated vaccine. Participants who received Pfizer vaccine yielded higher antibody titers than those who received AstraZeneca vaccine as a booster dose. This is a similar finding with other studies on the immunogenicity of Pfizer vaccine as the prime or booster dose.[5,6] In addition to boosting the heterogenous vaccine, the study revealed that after receiving 2 doses of AstraZeneca, the antibody levels to SARS-CoV-2 were adequately high. The result supported the Thai guideline which stated that the third dose was not required for at least 6 months in persons receiving 2 doses of AstraZeneca vaccine.[7] Currently, there are no studies to determine what antibody titer level detected is necessary to prevent SARS-CoV-2 infection.

We revealed that the interval between the second and the third doses of vaccines was associated to antibody titer level. This finding was consistent with previous data showing that the longer the interval between the first and second doses of AstraZeneca vaccine, the higher the antibody titer.[7,8] Although the younger age group seemed to have higher antibody titers than those of older age, it was not significant in the adjusted model.

This study used immunoassay to detect antibody to SARS-CoV-2 spike protein. We did not perform a neutralizing antibody test which determines the functional ability of antibodies to prevent infection by SARS-CoV-2 in vitro. However, the assay showed good agreement with virus neutralization assays.[9]

Regarding adverse reactions after the third dose of vaccination, there was no difference between group 1 and group 2. However, fever and headache were reported more frequently in participants of group 1. A similar finding was reported after the first dose of AstraZeneca compared to Pfizer vaccine.[5]

Limitations of this study are the absences of virus neutralization assays, cellular immunity assays and antibody titer levels before the third boosting dose of vaccine. In addition, the adverse reactions reported might be inaccurate since the data was collected retrospectively 2 months after the last dose of vaccination.

Conclusion

Although antibody testing is not recommended following vaccination,[10] our study supports the efficacy of current vaccination regimens for healthcare personnel in Thailand. Boosting AstraZeneca or Pfizer vaccine after two doses of inactivated vaccine and 2 doses of AstraZeneca are efficacious in producing immunity against SARS-CoV-2.

Acknowledgement

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Conflict of Interest

The authors declare no potential conflict of interest in this study.

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