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Comparison of COVID-19 vaccine's side effects between mRNA and inactivated virus vaccine for health workers

Badrul Munir, Widodo Mardi Santoso, Eko Arisetijono, Sri Budhi Rianawati, Fahimma Fahimma * and Helnida Anggun Maliga

Department of Neurology, Medical Faculty Universitas Brawijaya, Saiful Anwar General Hospital Malang, Indonesia.

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Abstract

Objective: Indonesian health workers mostly received three doses of vaccine, using two doses of inactivated viral vaccines, followed by the mRNA vaccine platform for the third dose. This study was conducted to investigate and compare the side effects of three vaccine doses using mRNA and inactivated viral vaccines platform for health workers.

Methods: Cross-sectional study was conducted on health workers who received three doses of the COVID-19 vaccine completely and willing to follow the research. Data collected were demographic characteristics, previous disease history, history of COVID-19 infection, and post-vaccination local and systemic side effects. Data was collected based on self-report and analyzed with a confidence level of 95% ($p < 0.05$).

Results: Overall, fifty-three participants received three consecutive doses of vaccine, consisting of two doses of inactivated viral vaccine (Sinovac) and followed by one dose of mRNA vaccine platform (Moderna). Post-vaccination side effects were more common after receiving the mRNA vaccine platform at 85% than after receiving the inactivated virus vaccine at 21%, with a significant difference for local swelling and all systemic side effects ($p < 0.05$). After administering the mRNA vaccine platform, local pain, muscle pain, and swelling at the injection site are the most frequent side effects. Patients with a history of COVID-19 infection had more frequent post-vaccination side effects compared to no history of COVID-19 infection (100% vs. 83%), and all of the local and systemic side effects were significantly different ($p < 0.05$). The most common side effects in patients with a history of COVID-19 infection are injection site pain, muscle pain, and swelling.

Conclusions: Post-vaccine side effects are mild and more common in mRNA vaccines platform than in inactivated virus vaccines. Post-vaccination side effects were higher in patients with a history of COVID-19 infection compared to naïve patients.

Keywords: COVID-19; Health Workers; Side Effect; Vaccine; mRNA Vaccine; Inactivated Virus Vaccine

1. Introduction

Vaccination programs to prevent the spread of COVID-19 disease have been carried out throughout Indonesia, mainly for health workers. There are several vaccine platforms used. Mostly, health workers received three doses of vaccine, using the inactivated virus vaccine platform for the first and second doses, followed by the mRNA vaccine platform for the third dose [1]. The provision of the third dose of vaccine with an mRNA platform is an effort to protect health workers because of the high transmission and death in Indonesian health workers even though they have received two doses of vaccine using an inactivated virus vaccine.

* Corresponding author: Fahimma Fahimma

The first and second doses of inactivated virus vaccine (Sinovac) had an effectiveness of 65.9% in preventing transmission, 87.5% prevented hospitalization due to COVID-19, 90.3% prevented ICU admission, and 86.4% prevented death [2]. Common side effects include injection site pain, fatigue, myalgia, headache, drowsiness, diarrhea, and fever [3].

While the third dose of mRNA platform vaccine (Moderna) had an efficacy of 94-95% after the second dose of vaccine, the side effects include local pain, swelling, heat in the injection area, and also systemic effects such as fatigue, fever, headache, myalgia, and arthralgia. Other effects that appear but are very rare include bell's palsy and hypersensitive [4]. However, the side effects of three vaccine doses on health workers with different platforms have not been widely publicized. In this study, we will evaluate and compare the side effects of vaccines with different platforms for health workers.

Objective

Comparing the side effects of mRNA and inactivated virus vaccine platform for health workers and evaluating post-vaccination side effects with a history of COVID-19 infection and naïve patients.

2. Material and methods

A cross-sectional study collected data from all Indonesian Neurological Association (INA) Branch Malang members who received the three doses of vaccine. The inclusion criteria were subjects who received the three doses of vaccine and were willing to follow the research, and we excluded the incomplete data. Data collected were demographic characteristics, including age and gender, previous history of the disease, history of COVID-19 infection, and post-vaccination local and systemic side effects. Data was collected based on self-reports and experience, through an online survey. The data collected were analyzed with Statistical Package for the Social Sciences (IBM SPSS Statistics, Version 25.0). The Chi-Square was used to compare the data, with a confidence level of 95% ($p < 0.05$). The study protocol was approved by the Ethical Committee of Perdossi Malang (approval No. 028/PERDOSSI-MLG/III/2021).

3. Results

Table 1 Basic data of study participants (n: 53)

		Result
Age (Years)	Mean (Years)	43 (25 – 70)
Sex	Male vs. Female	62 % vs 38%
Past Medical Illness	Allergy	7 (13%)
	Hypertension	5 (9%)
	Diabetes Mellitus	5 (9%)
Type of Vaccine	Inactivated Virus Vaccine (1st and 2nd dose)	53 (100%)
	mRNA Vaccine Platform (3rd dose)	53 (100%)
Second and Third Vaccine Period (month)	<3 months	4 %
	3-6 months	79%
	>6 months	17%
Side effects that appear (%)	mRNA Vaccine Platform	85%
	Inactivated Virus Vaccine	21%
History of COVID-19 infection	Positive Confirmation	28%
	Negative Confirmation	72%

A total of *fifty-three* data were obtained, with an average age of 42 years, and the majority of subjects were male (62% vs. 38%), history of past medical illness which are often found, among others allergy, hypertension, and diabetes. All

participants received the vaccine three times, with the inactivated virus vaccine (Sinovac) at the first and second doses and the mRNA platform vaccine (Moderna) at the third dose. The period between the second and third dose is generally 3-6 months (79%) and more than six months (17%). Table 1 shows the basic data of participants.

Post-vaccination side effects were more common after receiving the mRNA vaccine platform at 85% than after receiving the inactivated virus vaccine at 21%. The side effects often encountered after administering the mRNA platform vaccine are injection site pain, muscle pain, and swelling at the injection site. In comparison, an inactivated virus vaccine's most frequent side effects are fatigue, injection site pain, and muscle pain. Nevertheless, both vaccines had no severe side effects such as anaphylaxis or other severe systemic effects. There was a significant difference in swelling and all of the systemic side effects, including fatigue, joint pain, drowsiness, headache, fever, nausea and vomiting, redness, and chills between the mRNA vaccine platform and an inactivated virus vaccine, but no significant difference for injection site pain and muscle pain. Table 2 shows the comparison of mRNA and inactivated virus vaccine side effects.

Table 2 Comparison of mRNA and inactivated virus vaccine side effects

	mRNA vaccine (Moderna) N=53	Inactivated Virus Vaccine (Sinovac) N=53	p Value ^a
Injection Site Pain	48 (90%)	8 (15 %)	0.066
Muscle Pain	38 (72 %)	8 (15 %)	0.054
Swelling Injection site	28 (53 %)	0 (0%)	
Fatigue	23 (43 %)	9 (17 %)	0.000
Joint Pain	20 (38 %)	4 (8 %)	0.008
Drowsiness	14 (26 %)	8 (15 %)	0.000
Headache	19 (36 %)	3 (6 %)	0.017
Fever	12 (23 %)	5 (9 %)	0.000
Nausea and Vomiting	4 (8 %)	3 (6 %)	0.000
Redness	6 (11%)	1 (2 %)	0.005
Chills	13 (24 %)	0 (0%)	
Enlarged Lymph nodes	0 (0%)	0 (0%)	

^a Results of chi square test

Table 3 The basic data of patients with a history of COVID-19 infection and naïve patients

		History of COVID-19 Infection (N=15)	No History of COVID-19 Infection (N=38)	p Value ^a
Age (Years,mean)		44 (25 – 67)	43 (26 – 70)	0.155
Sex	Male vs. Female (%)	67% vs 33%	60.53% vs 39.47%	0.678
Past medical illness	Hypertension	3 (20%)	2 (6 %)	0.002
	DM	2 (13 %)	3 (8 %)	0.002
	Allergy	1 (7%)	6 (16 %)	0.205
Post-vaccine side effects (%)		15 (100%)	30 (83%)	0.054

^a Results of chi square test

Based on this study, 15 participants (28%) had a history of COVID-19 infection, while 38 participants (72%) had no history of COVID-19 infection. There is a significant difference between having a history of COVID-19 infection and no history of COVID-19 infection in terms of hypertension and diabetes mellitus, but no significant difference for allergy (Table 3).

From this study, Patients with a history of COVID-19 infection had more frequent post-vaccination side effects than patients with no history of COVID-19 infection (100% vs. 83%). The most common side effects include injection site pain, muscle pain, and swelling. These post-vaccination side effects were significantly different between groups with a history of COVID-19 infection and no history of COVID-19 infection. Table 4 shows the comparison of vaccine side effects after mRNA vaccine platform shots between patients with a history of COVID-19 infection and naïve patients.

Table 4 Comparison of vaccine side effects after mRNA vaccine platform shots between patients with a history of COVID-19 infection and naïve patients

	History of COVID-19 Infection	No History of COVID-19 Infection	p Value ^a
Injection site Pain	14 (93 %)	34 (90 %)	0.001
Swelling Injection site	12 (80%)	16 (42 %)	0.000
Muscle Pain	12 (80%)	26 (68 %)	0.000
Joint Pain	8 (53 %)	12 (32 %)	0.000
Fatigue	8 (53%)	15 (40%)	0.000
Chills	6 (40%)	7 (18 %)	0.000
Headache	5 (33 %)	14 (37 %)	0.000
Drowsiness	4 (27 %)	10 (26 %)	0.000
Nausea and vomiting	1 (7 %)	3 (8 %)	0.000
Enlarged Lymph nodes	0 (0%)	0 (0%)	

^a Results of chi square test

4. Discussion

This study compared the side effects of COVID-19 vaccination using an mRNA vaccine platform and an inactivated virus vaccine. Subjects who received the mRNA vaccine had a greater side effect of 80%, compared to 21% of the inactivated virus vaccine. There were significant differences, especially systemic side effects, between vaccine recipients with the mRNA vaccine platform and the inactivated virus vaccine. The most common side effects include localized injection pain, muscle pain, and swelling. These results are in line with a previous study that showed the side effects of the mRNA vaccine platform were other mild such as local pain, swelling, and local heat, in addition to systemic effects such as fatigue, fever, headache, myalgia, and arthralgia [4,5].

The high frequency of side effects of this mRNA vaccine can be related to the mechanism of the mRNA vaccine manufacturing process, the subject is exposed to pathogens such as glucose or capsid where the genetic RNA has a gene code that corresponds to the antigen. This RNA messenger is then translated by the host in the form of the relevant protein so that strong antibodies are formed. The process of protein formation is associated with many side effects [5].

While the mechanism of making inactivated virus vaccine is produced by activating the β -propiolactone-CN2 strain of SARS-CoV-2, which is assimilated from alveoli bronchial patients with the strain e 2019-nCoV-BetaCoV Wuhan/WIV04/2019, the process of inactivation of this vaccine has weaknesses, sometimes damage to antigens that cause the formation of immunity [6].

In our study, post-vaccination side effects were higher in patients with a history of COVID-19 infection compared to no history of COVID-19 infection. All of the local and systemic side effects were significantly different. This study is in line with previous studies, which showed that vaccine recipients with a history of COVID-19 infection reported more side effects than naïve patients, but not more severe ones. Vaccine systemic reactogenicity after the vaccine was more pronounced in people with pre-existing immunity [7].

The present study has several limitations. First, it was conducted on neurologists in Indonesia as representatives of health workers. Second, we did not correlate the time gap between vaccine shots time, vaccine side effects, and time of COVID-19 infection to provide more information. A need exists for more comprehensive and participatory studies.

5. Conclusion

Third dose vaccination with mRNA platform has more side effects, but no severe ones, than first and second dose vaccination with inactivated virus vaccine. The most common side effect of the third dose vaccines is local pain at the injection site. Post-vaccination side effects were higher in patients with a history of COVID-19 infection compared to no history of COVID-19 infection.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

The authors have no conflicts of interest to disclose.

Statement of ethical approval

This study was approved by the Ethical Committee of Perdossi Malang (approval No. 028/PERDOSSI-MLG/III/2021).

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

References

- [1] Hidayat R, Mustika AP, Avisha F, Djuliannisaa Z, Winari DD, Putri RA, et al. Surveillance of Adverse Events Following Immunization (AEFI) after Third Dose Booster Vaccination with mRNA-Based Vaccine in Universitas Indonesia Hospital Health Personnel. *Vaccines*. 2022; 10:877.
- [2] Jara A, Undurraga EA, González C, Paredes F, Fontecilla T, Jara G, Pizarro A, Acevedo J, Leo K, Leon F, Sans C, Leighton P, Suárez P, García-Escorza H, Araos R. Effectiveness of an Inactivated SARS-CoV-2 Vaccine in Chile. *N Engl J Med*. 2021 Sep 2;385(10):875-884
- [3] Al Kaabi N, Zhang Y, Xia S, Yang Y, Al Qahtani MM, Abdulrazzaq N, et al. Effect of 2 Inactivated SARS-CoV-2 Vaccines on Symptomatic COVID-19 Infection in Adults: A Randomized Clinical Trial. *JAMA - J Am Med Assoc*. 2021; 326(1):35–45.
- [4] Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. *N Engl J Med*. 2021; 384(5):403–16.
- [5] Anand P, Stahel VP. Review the safety of COVID-19 mRNA vaccines: a review. *Patient Saf Surg*. 2021; 15(1):1–9.
- [6] Kyriakidis, N. C., López-Cortés, A., González, E. V., Grimaldos, A. B., & Prado, E. O. (2021). SARS-CoV-2 vaccines strategies: a comprehensive review of phase 3 candidates. *NPJ vaccines*, 6(1), 28
- [7] Tissot N, Brunel A, Bozon F, Rosolen B, Chirouze C. Patients with history of COVID-19 had more side effects after the first dose of COVID-19 vaccine. *Vaccine*. 2021; 39(January):5087–5090 Contents.