

Lessons Learned from Global Administration of Sinopharm (BBIBP-CorV) Vaccine and Its Efficacy against COVID-19 in Older People

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ARTICLE INFO

Short Communication

VacRes, 2021

Vol. 8, No.2, 1-3

Received: October 25, 2021

Accepted: November 04, 2021

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KEYWORDS: COVID-19, Aged, Older adults, Sinopharm BBIBP-CorV

ABSTRACT

Sinopharm (BBIBP-CorV) is an inactivated whole-virus COVID-19 vaccine. The phase 3 trial showed an efficacy of up to 78% in preventing symptomatic COVID-19 infections. However, there have been questions raised regarding its efficacy in older people. In this paper, several pertaining lessons are highlighted. Firstly, there is a need to take into account the heterogeneity of COVID-19 vaccine studies, such as representation of older people; and whether the results are generalizable to the target population of immunization programs. Secondly, for older people, antibody responses alone may not indicate the level of protection provided by the vaccines, as cell mediated immunity is a better determinant of immunity in this age group. Finally, suggestions are given to improve the immune responses in older people, such as heterologous vaccination and booster doses.

Citation:

The COVID-19 pandemic due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is currently causing a global public health crisis. As of September 23rd 2021, the World Health Organisation (WHO) COVID-19 dashboard stated 229,858,719 confirmed cases and 4,713,543 deaths due to COVID-19 infections [1]. COVID-19 vaccines are an important public health approach to reduce the spread of infections and prevent complications and death. As of September 22nd 2021, 5, 874, 934, 542 vaccine doses have been administered globally [1]. The Sinopharm BBIBP-CorV vaccine is an inactivated whole-virus COVID-19 vaccine, manufactured by Beijing Bio-Institute of Biological Products Co Ltd. It was developed from a WIV04 strain, isolated from a patient in Jinyintan Hospital, Wuhan, China. The virus was cultivated in Vero cells, inactivated with β -propiolactone, purified and then adsorbed to 0.5 mg alum. The vaccine is available in pre-filled syringes with 0.5 mL phosphate-buffered saline without preservatives [2].

A phase 3 trial was carried out using this vaccine in the United Arab Emirates (UAE) and Bahrain in adults aged 18 years and older in which randomized 40382 participants received one of the two vaccines (WIV04 and HB02 strains) or an aluminium hydroxide-only injection, as a control. After a median follow-up of 77 days, these two vaccines demonstrated an efficacy of 72.8% and 78.1% against symptomatic COVID-19 infections [3]. Subsequently, the WHO approved BBIBP-CorV vaccine for emergency use [4]. However, several

questions have been raised regarding the Sinopharm vaccine in terms of efficacy, particularly in vulnerable groups such as older people. A study carried out in Peru among 400,000 frontline workers found that two doses of BBIBP-CorV vaccine was only 50.4% effective in preventing the infections [5]. In UAE, an independent study to determine the antibody levels among Sinopharm vaccine recipients found a lower antibody response, compared to the other COVID-19 vaccines, particularly among older people; mandating a booster dose for these patients [6]. A recent study from Hungary reviewed levels of virus neutralizing antibody titers after BBIBP-CorV and found that antibody production reduced significantly with age. In older people, 25% of those within 60 years and older to 50% of the vaccinated people over 80 years, did not produce protective antibodies [7]. In retrospect, the main phase 3 trial recruited a majority of participants between the ages of 18 to 59 years while older people were under-represented in the study [3].

These uncertainties that developed over a year highlight a few important lessons. Firstly, interpretation of vaccine efficacy studies should consider generalizability of findings to each target population. The exclusion criteria of studies should also be reviewed in terms of age, ethnicity and medical comorbidities [8]. For the currently available COVID-19 Phase 3 trials, there is some variability in the baseline characteristics of enrolled participants, including representation of older people in the studies. This is shown in Table 1 for Pfizer-

BioNTech (BNT162b2) [9], Moderna (mRNA-1272) [10], AstraZeneca (ChAdOx1 nCoV-19) [11], Janssen (Ad26.COV2.S) [12], Sputnik V (Gam-COVID-Vac) [13], and Sinopharm (BBIBP-CorV) vaccines [3].

Table 1. Baseline characteristics of study population of Phase 3 trials of COVID-19 vaccines.

Vaccine	Age ≥ 60 years	Female	Asian	Cardiac Disease	Pulmonary Disease	Diabetes Mellitus	Obesity
BNT162b2 (n = 37706)	15921 (42.2%) >55 years	18631 (49.4%)	1608 (4.3%)	553 (1.5%) MI + CHF	2931 (7.8%)	3163 (8.4%)	13218 (35.1%)
mRNA-1273 (n = 30351)	7512 (24.8%) ≥65 years	14366 (47.3%)	1382 (4.6%)	1496 (4.9%)	1454 (4.8%)	2875 (9.5%)	2046 (6.7%) Mean BMI 29.3
ChAdOx1 nCoV-19 (n = 11636)	1418 (12.1%) >55 years	11636 (60.5%)	517 (4.4%)	1241 (10.7%)	1360 (11.7%)	270 (2.3%)	Median BMI 23.5 (South Africa) 26.0 (Brazil)
Ad26.COV2.S (n = 43783)	14672 (33.5%)	19722 (45.0%)	1430 (3.3%)	1008 (2.3%)	437 (1.0%) COPD	3389 (7.7%)	12481 (28.5%) Mean BMI 27
Gam-COVID- Vac (n = 19877)	2144 (10.8%)	7708 (38.8%)	286 (1.4%)	Combined 4922 (24.8%)			BMI 26.75
Sinopharm (n = 38206)	612 (1.6%)	5945 (15.6%)	Mostly Asian countries	Excluded			BMI 26.9

There is also some heterogeneity in reporting between the different COVID-19 vaccine phase 3 trials. For example, some studies report obesity as the proportion of participants who are obese [9,10], while others report mean or median body mass index (BMI) in the results [3,11-13]. The Sputnik V study reported the number and proportion of people with concomitant diseases, such as diabetes, hypertension, ischemic heart disease and obesity, rather than in separate categories [13]. These differences in trials should be appreciated and considered during critical appraisal when deciding on vaccine selection for national vaccination programs.

For example, while the UAE study found limited antibody responses, another study performed in Sri Lanka found that 95% of those vaccinated with BBIBP-CorV seroconverted, including 93.3% for people age 60 years and older (compared to 98.9% in those age 20 to 39 years old) [14]. This available local data should support continued implementation and use of the Sinopharm vaccine in Sri Lanka, which may reflect different vaccine responses based on ethnicity. As further information becomes available, it may eventually reach the stage where clinicians should assess and individualize the selection of different vaccines for each patient, depending on their situation and preferences. Table 2 summarises the currently available studies on Sinopharm COVID-19 vaccine efficacy in different countries.

Secondly, there are specific considerations regarding vaccine efficacy in people. In older people, while immunizations generally generate less antibody responses than younger people due to immune senescence; antibody levels do not correlate well with immune protection against infections. Studies of influenza vaccine responses showed that measures of cell-mediated immune responses such as the ratio of IFN- γ to IL-10 and cytolytic mediators granzyme B levels better correlated with protection [15]. Furthermore, although antibodies provide protection against COVID-19 infections, a humoral immune response is not essential for controlling established infections; as seen in agammaglobulinaemia patients [16]. Thus, vaccine efficacy studies in older people

using immunological surrogate measures should measure both antibody and T-cell responses to gauge the potential level of protection in older people. Taking into account this lower immune response, the main goal of vaccination in older people is to provide some clinical protection against the disease, especially complications from severe disease or death. In other words, it is probably not feasible to expect to induce sterilizing immunity against COVID-19 infections in older people.

There should also be considerations in vaccine development on how to improve immunogenicity in older people. This is more important now with the appearance of new COVID-19 variants, which may render current COVID-19 vaccines less effective. A study measuring neutralizing activity from vaccine-elicited sera after BBIBP-CorV identified a complete or partial loss of efficacy by 12.13%, 20.97% and 24.26% for the lineages B.1.1.7, B.1.526 and P.1 respectively [17].

For each COVID-19 vaccine, this may include considering higher doses, adjuvants, and intradermal routes. These approaches managed to increase antibody titres in response to influenza vaccines by 82%, 52% and 32% respectively [18]. Heterologous vaccination with two different vaccine platforms may also elicit a better immune response [19], which is currently considered and tested in 'vaccine mixing' trials. Further knowledge is required before adopting this approach, as the order of vaccine administration may be relevant in inducing higher levels of neutralizing antibodies. For example, a pre-clinical study showed that while heterologous vaccinations were superior to homologous prime-boost vaccination with BBIBP-CorV or Ad5-nCoV, priming with an adenovirus vector vaccine, followed by a boost with inactivated virus, recombinant receptor binding domain (RBD) vaccine or mRNA vaccine resulted in the highest levels of neutralizing antibodies [20].

Table 2: Summary of studies related to Sinopharm COVID-19 vaccine efficacy in different countries.

Type of Study	Location	Trial Participants	Results
Phase 3 Randomised Controlled Trial	United Arab Emirates (UAE) and Bahrain [3]	40382 participants	Efficacy of 72.8% and 78.1% against symptomatic COVID-19 infections (Median 77 days)
Phase 3 Randomised Controlled Trial	Peru [5]	400000 frontline workers	Efficacy of 50.4% against symptomatic COVID-19 infections
Antibody Response	Hungary [7]	497 participants	75% seroconverted for age 60+; 50% for age 80+
Antibody Response	Sri Lanka [14]	282 participants	95% seroconverted (93.3% for age 60+ compared to 98.9% in 20-39 year olds)

In conclusion although there are arising concerns regarding the overall efficacy of the Sinopharm vaccine particularly in older people, more information is required regarding optimizing the use of available COVID-19 vaccines in different population groups and localities. There is also a need to improve development of subsequent vaccines to be more effective especially against the new variants.

ACKNOWLEDGEMENT

No research funding was obtained for production of this manuscript.

CONFLICT OF INTEREST

The author declares he has no conflict of interests.

REFERENCES

- World Health Organisation. WHO Coronavirus (COVID-19) Dashboard. [Internet]. 2021 Sep [cited 2021 Sep 24]. Available from: covid19.who.int
- Xia S, Duan K, Zhang Y, Zhao D, Zhang H, Xie Z, et al. Effect of an inactivated vaccine against SARS-CoV-2 on safety and immunogenicity outcomes: interim analysis of 2 randomized clinical trials. *JAMA* 2020;324(10):951-60.
- 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 randomised clinical trial. *JAMA* 2021;326(1):35-45.
- World Health Organization (WHO). Evidence Assessment: Sinopharm/BBIBP COVID-19 vaccine. [Internet]. 2021 Apr [cited 2021 Sep 24]. Available from: https://cdn.who.int/media/docs/default-source/immunization/sage/2021/april/2_sage29apr2021_critical-evidence_sinopharm.Pdf
- Silva-Valencia J, Soto-Becerra P, Escobar-Agreda S, Fernandez-Navarro M, Moscoso-Porras M, Solari L, et al. Efectividad de la vacuna BBIBP-CorV para prevenir infección y muerte en personal de salud, Peru 2021. Peru: Instituto Nacional de Salud. 2021 [cited 2021 Sep 24]: [23 p.]. Available from: <https://repositorio.ins.gob.pe/xmlui/bitstream/handle/INS/1318/Efectividad%20de%20la.pdf?sequence=1&isAllowed=y>
- Abu Dhabi Government Media Office. Department of Health – Abu Dhabi offers free Sinopharm vaccine booster dose to those eligible. 2021 May 29 [cited 2021 Sep 24]. Available from: <https://www.mediaoffice.abudhabi/en/health/departament-of-health-abu-dhabi-offers-free-sinopharm-vaccine-booster/>
- Ferenci T, Sarkadi B. Virus neutralizing antibody responses after two doses of BBIBP-CorV (Sinopharm, Beijing CNBG) vaccine. medRxiv 2021.07.15.21260362. doi: 10.1101/2021.07.15.21260362
- Teo SP. COVID-19 vaccine developments and considerations for appraisal of the evidence. *Pac J Med Sci.* 2021;21(2):33-35.
- Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med* 2020;383:2603-2615.
- 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;384:403-416.
- Voysey M, Clemens SA, Madhi SA, Weckx LY, Folegatti PM, Aley PK, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. *Lancet* 2021;397(10269):99-111.
- Sadoff J, Gray G, Vandebosch A, Cardenas V, Shukarev G, Grinsztejn B, et al. Safety and efficacy of single-dose AD26.COV2.S vaccine against Covid-19. *N Engl J Med* 2021;384:2187-2201.
- Logunov DY, Dolzhikova IV, Shcheblyakov DV, Tukhvatulin AI, Zubkova OV, Dzharullaeva AS, et al. Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia. *Lancet* 2021;397(10275):671-681.
- Jeewandara C, Aberathna IS, Pushpakumara PD, Kamaladasa A, Guruge D, Jayathilaka D, et al. Antibody and T cell responses to Sinopharm/BBIBP-CorV in naïve and previously infected individuals in Sri Lanka. medRxiv 2021. Doi: 10.1101/2021.07.15.21260621
- Teo SP. Review of COVID-19 vaccines and their evidence in older adults. *Ann Geriatr Med Res.* 2021;25(1):4-9.
- Cohen MS, Nirula A, Mulligan MJ, Novak RM, Marovich M, Yen C, et al. Effect of bamlanivimab vs placebo on incidence of COVID-19 among residents and staff of skilled nursing and assisted living facilities: a randomized clinical trial. *JAMA.* 2021;326:46-55.
- Zhang S, Yu X, Wei D, Xu W, Guo W, Li X, et al. Neutralizing activity of BBIBP-CorV vaccine-elicited sera against multiple SARS-CoV-2 variants of concern. *Res Sq* 2021. Doi: 10.21203/rs.3.rs-483022/v1.
- Ng TW, Cowling BJ, Gao HZ, Thompson MG. Comparative immunogenicity of enhanced seasonal influenza vaccines in older adults: a systematic review and meta-analysis. *J Infect Dis.* 2019;219:1525-1535.
- Choo SZL, Teo SP. Gam-COVID-Vac (Sputnik V): a heterologous adenoviral vector-based COVID-19 vaccine. *Aging Path Ther* 2021;3(2):43-45.
- He Q, Mao Q, An C, Zhang J, Gao F, Bian L, et al. Heterologous prime-boost: breaking the protective immune response bottleneck of COVID-19 vaccine candidates. *Emerg Microbes Infect.* 2021;10:629-637.
- Bar-On YM, Goldberg Y, Mandel M, Bodenheimer O, Freedman L, Kalkstein N, et al. Protection of BNT162b2 vaccine booster against Covid-19 in Israel. *N Engl J Med.* 2021. Doi: 10.1056/NEJMoa2114255
- Torbati E, Krause KL, Ussher JE. The immune response to SARS-CoV-2 and variants of concern. *Viruses.* 2021;13:1911.