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

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LESSONS LEARNED

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 infection 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 40,382 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 vaccine 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-
The ratio of IFN-γ to neutralizing antibodies provides protection against COVID-19 infections, a finding that 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-elicted sera after BBIBP-CorV identified a complete or partial loss of efficacy by 12.13%, 20.97% and 24.26% for the lineages B1.1.526 and P.1 respectively [17].

Table 2 summarises 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 mediatory 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 agammaglobulinemia 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-elicted sera after BBIBP-CorV identified a complete or partial loss of efficacy by 12.13%, 20.97% and 24.26% for the lineages B1.1.7, 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.

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

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.

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CONFLICT OF INTEREST

The author declares he has no conflict of interests.

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