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Original Article

Expected response to the additional third dose of COVID-19 vaccine based on different complete standard vaccination background

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Abstract: COVID-19 vaccination is proven useful for primary prevention against COVID-19. Classically, two doses of vaccine are required. After complete vaccination, there might be a decline in immunity level. When there is a new emerging variant and a possible decline of immunity in general people after standard mass vaccination, many scientists propose ideas for the additional third dose vaccination. The effectiveness of the third vaccine still unknown, therefore any studies on its effectiveness are interesting. Additionally, there are also many new ideas for using a new type of COVID-19 crossing to the previous completely vaccinated one. In this study, the authors use a clinical model technique for estimating of response to the additional third dose of COVID-19 vaccine based on different complete standard vaccination background.

Keywords: COVID-19, vaccine, third, dose

Introduction

COVID-19 is still a global crisis and there is still no successful disease control [1]. Vaccination is the hope for management of crisis [2]. At present, COVID-19 vaccination is accepted as a useful primary prevention against COVID-19. Classically, two doses of vaccine are required for complete vaccination. However, there might be a decline in immunity level after complete vaccination and self-protection behavior is still needed.

When there is a new emerging variant and a possible decline of antibody after completeness of standard vaccination, many scientists propose ideas for using an additional third dose of COVID-19 vaccine [3-5]. The effectiveness of the third vaccine still unknown, therefore any studies on its effectiveness are interesting. Additionally, there are also many new ideas for switching to a new type of COVID-19 to the previous completely old type vaccine. In this study, the authors use a clinical model technique for estimating of response to the additional third dose of COVID-19 vaccine based on different complete standard vaccination background.

Materials and methods

The present study is based on clinical mathematical modeling technique. The technique is a standard in silico mathematical modeling technique and has been proven no interference from environmental confounding factors as in vitro or in vivo studies. Primary data refer to basic information on protective efficacy rates of different types of vaccine [6]. A basic assumption is different vaccines have a different immunogenicity mechanism. Different vaccines based on different biotechnologies have different basic components and result in different immunoprotection inductions. After completeness of standard vaccination, there will be the most effective immunity level or protective efficacy before declining occurs. The extra third dose will be used as a booster. The effect of the third dose is calculated using basic data on the protective efficacy, or boostering effect, caused by each vaccine's second dose. The boostering activity is supposed to be the vac-

Table 1. Clinical modelling for the third dose COVID-19 vaccination

The background complete two dose vaccination	The third dose vaccine		Protective efficacy rate (%)	
	Type	Specific boostering* activity (%)	Background protective effect after the second dose** (%)	Expected Protective efficacy rate after the third dose (%)
Inactivated	Inactivated	27	86	86
	Viral vector	37	86	89
	mRNA	24	86	94
Viral vector	Inactivated	27	89	86
	Viral vector	37	89	89
	mRNA	24	89	94
mRNA	Inactivated	27	94	86
	Viral vector	37	94	89
	mRNA	24	94	94

*Specific boostering activity means ability to increase protective efficacy rate to the first dose of vaccine if that vaccine is given as the second dose. **Background protective effect after the second dose means the reported immunoprotection rate after complete two dose vaccination of that vaccine.

cine's ability to increase protective efficacy after the second dosage when compared to the first dose for modeling purposes.

For modelling, it is primarily assumed that after the second dose, the protective efficacy will be used as background protective efficacy. Conceptually, the additional protection from the third dose can increase boostering activity, improve the protective efficacy rate, in case that it is given as the second dose but it will not exceed the background protective efficacy. If there is a switching type of vaccine, the additional protection from the third dose will equal to the reported protective efficacy of the switched brand vaccine in case that it is used as the boostering for its type corresponding first dose. However, as an important condition for present modeling, the final protective efficacy will also not exceed the background protective efficacy of that new switched vaccine. Hence, the efficacy of the third dose will be equal to the background protective efficacy from the complete the second dose of standard vaccination. Final expected protective efficacy rate after the third dose will be calculated by "background protective effect after the second dose + additional protection from the third dose", under the earlier mentioned primary condition.

Results

According to the clinical modeling, the results are shown in **Table 1**. It can show that the expected effect of switching is various, either increasing or decreasing protective efficacy. This confirms that it is still required further studies to evaluate the effect of switching. In the lack of clinical data, the switching of vaccine brand should not be considered if it is not necessary. Based on the model, different expected outcomes from different third dose vaccination alternative are observed. From any complete vaccination background, the third dose COVID-19 vaccination with mRNA vaccine can result in the most expected protective efficacy.

Discussion

Declining of immunity after COVID-19 vaccination is reported and it becomes a concern for the repeated infection. After complete 2 doses of vaccination, COVID-19 infection is still possible and it is necessary for prevention. Additionally, the immunity in some specific groups such as dialysis case is not good after complete two doses of vaccination. Hence, the ideas for using the third dose of vaccination are proposed [3-5]. There are few reports on the usefulness of the third dose of vaccine and it is usually with specific populations with immune impairment status [7]. Many researchers presently conclude that the third vaccine dose can boost immune response, but it may not be needed [8].

In addition, in some areas, the vaccination is various. Different protective efficacy rates of different types of vaccine are reported [6]. A switching and matching of vaccine brand might

be used [9]. This is also a possible practice for the third dose of vaccine. For the third dose, the old vaccine type or switched new vaccine type might be selected depending on local policies.

Collecting data from a clinical trial needs a long time. Furthermore, utilizing a non-standard immunization approach raises ethical concerns. According to the most updated data at the end of October 2021, there is a report from Israel showing that the third dose of the mRNA COVID-19 vaccine might be effective in protecting individuals against severe COVID-19, compared with receiving only two doses [10]. Similarly, Gilboa et al. reported that the third dose of mRNA COVID-19 vaccine could induce good immunity among elderly vaccine recipients [11].

In this study, the outcomes are concordant with the recent studies. In this report, a clinical modelling technique is used for simulating different situations, which were not studied in recent studies. Without brand switching, the third dose of vaccination can act as a boostering to achieve the highest protection level. Regarding brand switching, it might help increase the protective efficacy if a good combination is selected. Interestingly, the expected usefulness of the third vaccination is detected by using mRNA COVID-19 vaccine. The result from the present clinical modeling study can confirm the recent observation from Israel [10, 11].

Disclosure of conflict of interest

None.

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