Short Communication
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Heterologous COVID-19 Vaccination; Sinopharm and Pfizer-BioNTech

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Abstract
This short communication and highlights is the first one talking about receiving two different Anti-COVID-19 vaccines in full doses. In a small group of almost medical personals in Duhok city, Kurdistan region of Iraq, for the first time in the world 15 doctors who were vaccinated with two doses of Sinopharm at early March were revaccinated with two doses of Pfizer-BioNTech after approximately 5–6 months. They were developed a good immune response without serious side effects so far. This will direct us toward potential safety protocol of mixing full doses of different vaccines at least in the short term. No serious side effects in the short term had been registered in this new combination. Such policy might open ways for further larger studies for taking different Anti-COVID-19 vaccines in full doses.
Keywords: COVID-19, COVID-19 vaccine, mixing vaccines, Pfizer-BioNTech, Sinopaharm, heterologous vaccination

Introduction

After the emergency of the novel, infectious, SARS-CoV-2 virus, responsible for COVID-19, and the declaration of pandemic state, finding a vaccine that can stop the spread of the virus became of paramount importance. Pfizer-BioNTech, AstraZeneca/AZD1222 (AstraZeneca), Janssen/Ad26.COV 2.S (Johnson & Johnson), Moderna, and Sinopharm are among the available vaccines which are currently in use for protection against COVID-19 disease.[1]

With the introduction of the COVID-19 vaccine, for the establishment of the full protection, the usual vaccination strategy was carried out with each recipient complete all doses of the same vaccines; most authorized vaccines require two doses administered weeks or months apart. However, due to the short supply and the unforeseen side effects of the vaccines, an unproven strategy was placed into action by some countries; including Canada and several European countries. The new strategy is characterized by recommending a different vaccine as the second dose; switching shots midstream.[2]

Currently, researchers are directing their attention toward the heterologous prime-boost vaccination against COVID-19.[3] With the shortage in the supplies and in the light of changing recommendations regarding the use of AstraZeneca vaccine, countries are now advising a heterologous prime-boost schedule with an alternative vaccine as the second dose for the individuals previously primed with AstraZeneca; Pfizer-BioNTech is more commonly recommended.[4]

Methods and Results

This short communication is based on notion of taking two different vaccines specifically Sinopharm and Pfizer. Its main methods depend on conceptual conclusion of mixing two vaccines in full doses in 6 months apart.

Although the evidence on the effectiveness and safety of heterologous vaccination remains limited, some of the European countries recommended the use of the heterologous regimes due to safety concerns.[3]

Researches on the application of the heterologous vaccination strategy for Sinopharm vaccine as the prime and Pfizer as the boost are yet not available. Yet, with the previous findings for AstraZeneca and Pfizer, Sinopharm can be in line and could show almost similar results. However, the possible complications should not be ignored as inducing immunity by various methods could possibly lead to developing more severe side effects[4] or even auto-immune diseases.

In a small group of almost medical personals in Duhok city, Kurdistan region of Iraq, for the first time in the world 15 doctors who were vaccinated with two doses of Sinopharm at early March were revaccinated with two doses of Pfizer after approximately 5 months. They were justified this action by their own decision and knowledge based on minimal titer of formal vaccine antibodies production and travel restrictions on Sinopharm vaccinated people. Then after receiving two doses of Pfizer-BioNTech they were developed immune response without recorded serious side effects. This will direct us toward safety protocol of mixing full doses of different vaccines at least in short term.

Discussion

The newly enlightened, heterologous COVID-19 vaccination, strategy is widely spreading. According to Sander "The mRNA vaccines are really, really good at inducing antibody responses, and the vector-based vaccines are better at triggering T cell responses", hence, the immune system might be given more than a single way to recognize a pathogen by mixing two types of vaccines.[3]

The recent studies are not perfectly reliable to assess the actual protection against COVID-19 since patients are not followed for infection post vaccination.[2] Yet, the idea is quite taking a turn to spread. With the absence/limited data on the reactogenicity, safety and immunogenicity of such schedules, it's not yet been recommended globally and remains an idea under investigation used only on need in order to mitigate the against supply shocks or shortage; to fulfill the speed of vaccination.[4] The three basic stones of any vaccine, i.e. reactogenicity, safety and immunogenicity, remains under investigation with the heterologous vaccine schedules.

In a heterologous vaccine schedules study trial, self-reported solicited local and systemic symptoms showed a

greater systemic reactogenicity following the booster dose than their homologous counterparts, the incidence of feverishness reported in the study was as follow: was BNT for prime and ChAd for boost (41%), ChAd for prime and BNT for boost (34%), BNT for both prime and boost (21%) and ChAd for both prime and boost (10%), nevertheless, no difference was encountered in the hematology and biochemistry profiles between heterologous and homologous vaccine schedules.[4]

The phase 2 trial of Alberto Borobia and colleagues, administration of Pfizer vaccine as the second dose for the prime AstraZeneca, assessed the immunogenicity and reactogenicity; a robust immune response and mild reactogenicity was noticed following the administration of Pfizer vaccine as the second dose 8–12 weeks after the first dose of AstraZeneca.[3,5] The study showed promising results regarding immunogenicity; 14 days after the second dose of Pfizer, 100% of the participants showed neutralizing antibodies. Yet, the safety was not fully assessed due to the small sample size and short follow-up.[3]

Despite the confounding factors, a study on the immunogenicity of heterologous vaccination with ChAd as prime and BNT as booster dose revealed a stronger immune response than the homologous vaccination with ChAd. Additionally, individuals vaccinated with BNT/BNT and ChAd/BNT had similar degrees of neutralizing antibodies 2–3 weeks after booster dose.[6]

With this new strategy, further analysis should be made to determine the best choice for the prime and boost in the heterologous vaccination; antibody response with Pifizer as prime and AstraZeneca as boost was lower than AstraZeneca as prime and Pfizer as the boost. The T-cell response was found to be higher in mixed vaccines, highest with the latter, than the homologous vaccination. Nevertheless, two-doses of Pfizer showed the best antibody response.[3,7]

Worries about the effectiveness of the Sinopharm vaccines emerged with individuals showing low antibody titer following vaccination.[8] The low antibody production was more pronounced with increasing age; numerous subjects above the age of 65 were found not to produce any protective antibodies, reaching 50% for older subject.[9]

Travel restrictions to western countries on Sinopharm vaccinated travelers started to be an emerging issue. With the European Union implying a similar ban, the Sinopharm vaccine recipients will be forced to be vaccinated with other vaccines, Pfizer for instance, hence, the vaccination regime will be forced toward heterogenic vaccination.[10] Both travel restriction on Sinopharm vaccinated travelers with the possible low antibody titer being noticed could direct the application of heterogeneous vaccination by the authorities. Additionally, with trials on going for further supporting the heterologous vaccination,[11] Sinopharm as prime vaccine with a different boost, Pfizer for example, should be regarded and not spared from the upcoming trials as a large proportion of populations have already received Sinopharm vaccine.

The principle of the emerged Mix and Match COVID-19 vaccination idea was the hope for a stronger, more robust immune responses trigger in addition to simplify the immunization efforts in the face of fluctuating supplies of various vaccines.[12] The heterologous schedule is drawing the attention for several reasons including; logistical considerations and clinical efficacy, an opportunity to make vaccination programs more flexible in response to fluctuations in supply, potential to produce a stronger response.[3,13]

The success of heterologous vaccination regimes will provide an opportunity for to speed up the vaccination campaign worldwide and maximize the impact on COVID-19 pandemicity.[13] Recent studies show the impact of heterologous dosing with improved immunogenicity and possible superiority over the homologous regime. Additionally, advantageous immunogenicity outcomes, humoral and cellular responses to the original SARS-CoV-2 and its variants, have been demonstrated by this strategy.[3,14,15]

Moreover, immunocompromised patients, patients with malignancy, transplantation or receiving immunosuppressant's, may particularly benefit from enhancing immunity via heterologous vaccination that combination of two vaccines can offer complementary stimulation of different immune pathways; long lasting B cell and potent T cell responses.[14,15]

In a small study, the neutralizing activity against SARS-CoV-2 variants was assessed by comparing a homologous and a heterologous boost; robust inhibition of SARS-CoV-2 variants, including delta variant, was noticed. With the strong immune response following heterologous vaccination, despite the limitations, researchers suggest heterologous vaccination as a suitable strategy to restrain SARS-CoV-2 variants.[13,16,17]

Conclusion

Up to this moment the heterologous vaccines administration is a reasonable option without serious side effects. Different type of vaccines including conventional-made vaccine like (Sinopharm) and RNA-based vaccine (Pfizer-BioNTech) can be an exciting notion.

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None.

Conflicts of Interest

The authors declare no conflict of interest.

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