



Commentary

SARS-CoV-2 vaccination for immune-comprised patients: More is required

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The two-dose BNT162b2 (Pfizer–BioNTech) and mRNA-1273 (Moderna) are among the common used vaccines against SARS-CoV-2, with the estimated effectiveness for preventing COVID-19 after the second dose above 90% [1,2]. Immune-comprised populations, including solid-organ transplant recipients are typically excluded from trials investigating COVID-19 vaccines, though they are at increased risk for severe SARS-CoV-2 infection [3,4].

It is gratifying that Julian et al provided a comprehensive understanding of both humoral and cellular immune response after vaccination with the BNT162b2 and mRNA-1273 in dialysis patients and kidney transplant recipients (KTR) in this Issue of The Lancet Regional Health – Europe [5]. Seroconversion was tested with the SARS-CoV-2 NeutraLISA and the level of cellular immunity level was evaluated by the interferon- γ release assay or flow cytometry. They revealed that compared with a relatively healthy population, the seroconversion and cell-mediated immunity induced by the SARS-CoV-2 vaccine in KTRs are at a much lower level. However, the immunological efficacy of the SARS-CoV-2 mRNA vaccine in the dialysis patients were only slightly influenced. Meanwhile, they suggested that the poor efficacy of the SARS-CoV-2 vaccine in KTRs might be influenced by type and number of immunosuppressive drugs as well as the vaccine types [5]. The results are consistent with Boyarsky's recent finding that only 54% of the solid organ recipients showed detectable antibodies even after the second dose of mRNA SARS-CoV-2 vaccine and those receiving antimetabolites showed even worse antibody response [6].

But there are still quite a lot of problems waiting to be solved regarding to the vaccination against COVID-19 among immunodeficiency population. First, in addition to CD4+ T cells, CD8+ T cells also play a significant role in the defense and activation of immune response post-vaccination, and the longitudinal variation and detailed features of CD8+ T-cell response remain uncertain. Second, the vaccination-related seroconversion of antibody or T cell immune response doesn't equal to sufficient immune protection against subsequent infection [7]. In the study, though capacity against infection of the two vaccines in KTRs was assessed, no concrete conclusion could be drawn due to the limitation of sample size and short follow-up time. In a recent real-world study, the effectiveness of the BNT162b2 mRNA vaccine in immunodeficiency people including solid organ recipients is indeed lower than in healthy population, with 90% against documented infection and 84% against symptomatic infection [8]. However, the immunodeficiency population includes a large group of heterogeneous populations, and future research needs to be further refined and stratified.

Though with limitation, all these data hint that the effectiveness of SARS-CoV-2 mRNA vaccine was comprised in immunodeficiency population and the standard two-dose mRNA vaccine was not able to provide enough protection. It is encouraging to try additional booster dose of vaccine to improve COVID-19 vaccine responses in immunodeficiency population. In a recent case series, 30 solid organ recipients who had a suboptimal response to standard vaccination were given a third dose of vaccine. Antibody titers increased after the third dose in one-third of patients with negative antibody titers or low-positive antibody titers [9]. The scientific problem of whether additional dose will increase the vaccination-related immune response and improve the clinical effectiveness still needs to be verified by large-scale clinical trial. Further, we also need to investigate the duration of the immunological memory to SARS-CoV-2 after vaccination and its association with host's immune status.

In addition to efficacy, the safety of vaccines should not be ignored. Julian et al found hospitalization due to vaccination happened to 1.6% (6/376) of the KTRs and 0.4% (5/1304) of the dialysis people. Whether the mRNA vaccine is safe in the immunodeficiency still needs further investigation, especially in the cases that potentially require additional vaccination. It has been suggested that systemic events such as fever, fatigue, headache, chills, were more often after receiving the second dose of either the BNT162b2 or mRNA-

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E-mail address: caobin_ben@163.com (B. Cao).<https://doi.org/10.1016/j.lanep.2021.100191>2666-7762/© 2021 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

1273 vaccine than after receiving the first dose [1,2]. If immunodeficiency patients need to be vaccinated with a larger or additional dose of vaccine to obtain immune protection, caution should be taken that the side effects might increase extremely. Further large randomized controlled trials and real world studies are needed to validate the effectiveness and safety of additional booster dose of vaccine in the immunodeficiency patients.

In conclusion, immunodeficiency patients including solid organ recipients are at higher risk of severe or critical COVID-19 and they are the main targets needing vaccine protection. However, the standard two-dose mRNA vaccine was not able to provide them sufficient protection. More data is required to revise the vaccination policy in these patients.

Contributors

Hui Li, Jiapei Yu and Bin Cao drafted the comments together.

Declaration of Interests

No potential conflict of interest exists for all the authors.

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