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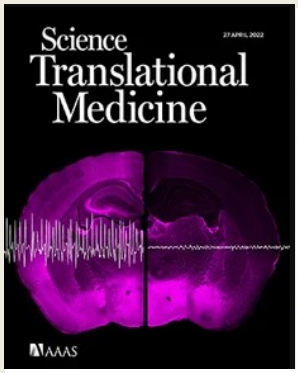

RESEARCH ARTICLE | CORONAVIRUS

Infection or a third dose of mRNA vaccine elicits neutralizing antibody responses against SARS-CoV-2 in kidney transplant recipients

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STM: How to reduce breakthrough infections in repeated non-responders to COVID-19 vaccinations?

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To The Editor:

Transplant recipients, who receive immunosuppression medications to prevent graft rejection, are characterized by high COVID-19–related mortality and defective response to COVID-19 vaccinations.

Post-vaccination serological testing (PVST) plays an important role in the control of non-responders to vaccine. For hepatitis B, the Centers for Disease Control and Prevention (CDC) recommended PVST using the World Health Organization (WHO) International Standard (IS) for immunocompromised individuals before and after hepatitis B vaccination. For repeated non-responders (anti-HBs antibody <10 mIU/mL, the WHO IS 07/164) to hepatitis B vaccination, anti-hepatitis B antibody injections are recommended if exposed to hepatitis B virus [1].

In December 2020, WHO issued an urgent request for the quantification of anti-SARS-CoV-2 immunoglobulin for PVST due to SARS-CoV-2 vaccine breakthrough infection. The WHO IS (20/136) provides a unified benchmark for effective & protective antibody evaluations after COVID-19 vaccination [2].

Charmetant and colleagues first described an important study of 62 renal transplant recipients that did not have neutralizing anti-RBD IgG after two doses of mRNA BNT162b2 vaccine [3]. 39% of second-dose non-responders produced anti-RBD IgG after the third dose of mRNA vaccine. However, there were 61% of non-responders to the third dose vaccine with a risk of the breakthrough infection.

Caillard and colleagues further reported a cohort of 92 renal transplant recipients who did not have anti-spike IgG (< 143 BAU/mL) after the third dose of mRNA vaccines [4]. However, there were 52.9% of non-responders to BNT162b2 vaccine and 48.3% of non-responders to mRNA-1273 vaccine after the fourth dose of mRNA vaccines. These all demonstrate the importance of PVST to assess the impact of repeated non-response to the SARS-CoV-2 vaccine. These non-responders, who received the SARS-CoV-2 vaccine at the third or at the fourth dose without PVST monitoring, may relax extra precautions without masks and, if infected, may become severe COVID-19 with poor outcomes.

To address the cutoff value of PVST using the WHO IS, Zeng and colleagues reported clinical results from people after the SARS-CoV-2 vaccination in the general population [5]. PVST has identified individuals with inferior immunity in the general population. There were 7.5–11.7% of non-responders to the COVID-19 vaccination in the general population. An individual with a titer of anti-SARS-CoV-2 spike IgG that is below 50 BAU/mL with the WHO IS (20/136) is considered a non-responder to COVID-19 vaccination at 30–90 days after the last vaccine dose.

There are several FDA-approved serological tests with WHO IS available. Physicians can follow the WHO-recommended PVST to reduce mortality in transplant recipients. There are existing countermeasures (such as an N95 mask), FDA-approved anti-SARS-CoV-2 immunoglobulin and/or FDA-approved antiviral treatments for repeated non-responders in transplant recipients following SARS-CoV-2 vaccine breakthrough infection [5].

In conclusion, above studies are a clear warning sign that transplant recipients may be vulnerable to breakthrough infection that results in indigent outcomes. There is an urgent need for further analysis and research to elucidate the potential role of PVST using the WHO IS to accelerate protection of our unprotected patients and save their lives.

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