

SARS-CoV-2 vaccination in haemodialysis patients: Insides from a prospective study comparing mRNA and viral vector vaccines

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Nearly three years into the pandemic, COVID-19 has led to vast changes in our lives, having a large impact on morbidity and mortality especially among vulnerable patient populations such as those with end-stage kidney disease.¹ We have witnessed the rise of unprecedented vaccines developed with the combined effort of the medical society in no time. Overall, they contributed to reduce morbidity and mortality. Clinical approval studies however excluded high-risk populations such as haemodialysis patients. So far, only smaller studies have investigated either humoral antibody response or clinical effectiveness after SARS-CoV-2 vaccination within this group. Larger cohorts simultaneously analyzing serological and clinical effectiveness especially after the application of different vaccine types are still needed.

In the current issue of *The Lancet Regional Health – Europe*, Martin and colleagues² report the results of a prospective observational study which compared the immunogenicity and clinical effectiveness of two doses of mRNA-based (BNT162b2) versus two doses of viral vector (ChAdOx1) SARS-CoV-2 vaccines within a large cohort of 1021 haemodialysis patients in the UK. 523 (51%) patients received BNT162b and 498 (49%) patients received ChAdOx1. Almost half of the patients (45.7%) had evidence of prior infection before vaccination. Humoral response was assessed with measurement of anti-spike antibodies; T cell response was analyzed in a subgroup of 191 patients (19%). During the study period, rigorous testing was performed with weekly nasopharyngeal swab PCR tests and anti-nucleocapsid serology to detect breakthrough infections. 84 patients who refused vaccination served as a reference group. Serological responses after a third booster

vaccination with BNT162b2 were assessed in 507 patients without breakthrough infections.

The study is one of the largest to compare viral vector and mRNA vaccines against SARS-CoV-2 in haemodialysis patients. Its particular strength lies in the combination of antibody measurement and rigorous COVID-19 infection monitoring to establish vaccine effectiveness. The study found comparable high seroconversion rates of 91.7% between both vaccine types. Overall T cell response was poor. Previous COVID-19 infection was associated with significantly higher antibody response, immunosuppressive treatment with lower antibody concentrations. These results support the findings of numerous smaller studies using mostly mRNA vaccines in haemodialysis patients: a favorable, albeit diminished early antibody response with lower antibody levels compared to healthy controls; higher antibody levels in patients with previous COVID-19 infection and an inverse correlation with systemic immunosuppression; higher antibody levels with mRNA vaccines (mRNA-1273 > BNT162b2 > ChAdOx1); declining antibody titres within 6 months of vaccination, and a good response after booster vaccinations.²

Although ChAdOx1 led to significantly lower anti-spike antibody levels, both BNT162b2 and ChAdOx1 vaccines showed comparable clinical benefit, with high effectiveness in preventing hospitalization by 77% (rate per 1000-patient days: 0.33 vs. 0.09) and death by 93% (rate per 1000-patient days: 0.22 vs. 0.038) related to COVID-19 in the real-world setting. These results go in line with previous studies.³ Vaccine effectiveness to prevent an infection was expectedly lower (53%). Patients with low or without antibody response after the second vaccine dose were at higher risk of breakthrough infections as reported by others.⁴

Anti-spike antibody titres significantly increased after a third mRNA booster vaccination which has been confirmed by several studies.^{5–7} Antibody titres remained significantly higher after homologous mRNA vaccination compared to heterologous vaccination. A first SARS-CoV-2 booster significantly increases the humoral antibody response in hemodialysis patients as well as in the general population and is now considered an essential part of the vaccine strategy.¹

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The following decline in antibody titres can be successfully reversed with a second booster dose.^{5,6,8,9} Nevertheless, adaptation of vaccine strategies for haemodialysis patients is warranted. Patients with prior COVID-19 infection elicit significantly higher antibody responses. In this case, a booster vaccination could be postponed, whereas patients with poor antibody response might benefit from earlier booster vaccinations. This argues in favor of regular assessment of quantitative antibody titres, while further studies need to establish protective antibody thresholds.

However, with the emergence of new virus variants the picture has changed. The Omicron variant has demonstrated significant immune evasive properties with higher rates of breakthrough infections despite primary and booster vaccinations. Nonetheless, mortality is significantly lower compared to previous variants. As current vaccines elicit a decreased humoral and cellular immune response against Omicron compared to SARS-CoV-2 wild type even after 4 doses,¹⁰ we are looking forward to the approval of Omicron-adapted SARS-CoV-2 vaccines.

What can we learn for the implementation of other vaccinations in high-risk populations, e.g., patients with end-stage kidney disease or immunosuppressive therapy? Regular assessment of vaccine responses, either using antibody measurement and/or cellular responses should become routine clinical practice. Adopting vaccination strategies with higher vaccine doses or multiple dosing for non-responders should be considered, the latter already having been established for hepatitis B vaccination. Further studies need to determine protective thresholds and booster schedules for COVID-19 and other vaccines, depending on their clinical benefit.

Contributors

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Declaration of interests

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