RESEARCH LETTER

Waning but persistent humoral response 6 months after the third dose of the mRNA BNT162b2 vaccine in hemodialysis and peritoneal dialysis patients

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Patients receiving maintenance dialysis have a diminished humoral response to SARS-CoV-2 vaccination, which led the French National Authority for Health to recommend, in April 2021, a third dose in the first set of vaccination in this population. If the third vaccine dose substantially increased antibody (Ab) levels in dialysis patients [1–3], the long-term durability and the robustness of a protective humoral response against SARS-CoV-2 remains unknown.

We assessed the dynamics of the humoral response of both hemodialysis (HD) and peritoneal dialysis (PD) patients from the Nephrology Department of the Centre Hospitalier Sud-Francilien (Corbeil-Essonnes, France), before and at one (M1), three (M3) and six (M6) months after a third dose of the mRNA BNT162b2 vaccine (Pfizer-BioNTech®). Patients with a history of symptomatic COVID-19 or with asymptomatic COVID-19 after the third dose, patients without serology results at M1 or M6, and those who received a kidney transplant, or died were excluded (Figure S1).

Humoral response was evaluated by measuring the plasma concentrations of anti-SARS-CoV-2 spike protein S1 total immunoglobulin antibodies using the Roche Elecsys® immunoassay [4]. According to the manufacturer’s protocol, patients with an anti-spike antibody titer below 0.8 AU/mL were classified as seronegative. An anti-spike antibody titer below 257 AU/mL—corresponding to the threshold of the WHO International standard unit of 264 binding antibody units [BAU]/mL [5] which offers 80% protection against symptomatic COVID-19 [6]—was classified as a low antibody titer. The kinetics of the humoral response was assessed as the ratio of the difference in anti-spike antibody titer between M1 and M6, over the titer at M1, and expressed in percentage. Clinical and biological data were collected as previously detailed [1]. Anti-nucleocapsid serology was also systematically performed before the third vaccine dose. Wilcoxon and Fisher’s exact tests were used to compare quantitative and qualitative variables, respectively. Wilcoxon signed rank test was used to analyze the paired data. Statistical analyses were conducted using R® 3.6 and GraphPad Prism® softwares.

Sixty-eight patients (n = 34 HD and n = 34 PD) were included, with a dialysis vintage of 3.0 [interquartile range, IQR: 1.0; 6.0] years (Table S1). Median age was 66.0 [53.8; 76.3] years, 65% were men and 18% had a history of immunosuppression. After 6-month follow-up, the anti-spike antibody titer significantly decreased from 6924 [1903; 11485] AU/mL at M1, to 2035 [597; 4009] AU/mL at M3, and to 875 [290; 1979] AU/mL at M6 (p < 0.0001) (Figs. 1, S2), corresponding to a median decrease in anti-spike antibody titer of 84.3% [75.5, 88.0] between M1 and M6.

The rate of patients with a low antibody titer (i.e., < 257 AU/mL) increased from 8.8% at M1 to 25% at M6, but no patient sero-reverted with 67 seropositive patients (98.5%) at M6. Compared with patients with an antibody titer ≥ 257 AU/mL at 6 months, those with an antibody titer < 257 AU/mL were older, were more likely to have
a history of immunosuppression, had a lower antibody titer before and one month after the third vaccine dose, and lower serum gamma globulin and albumin levels (Table S1). Humoral response was not different between HD and PD patients (Table S2). Patients with positive anti-nucleocapsid serology incidentally found before vaccination, had a higher titer and a lower decrease in Ab titer at M6 (Table S3).

This is the first description of the 6-month kinetics of humoral response after the third vaccine dose against SARS-CoV-2 in dialysis patients. Our data show a waning humoral response over time, with a median decrease in antibody titer of 84.3% in 6 months and a rate of patients with low antibody titer increasing from 8.8 to 25% between M1 and M6. However, median anti-spike antibody titer remained more than threefold higher 6 months after than before the third dose, with a seropositivity rate of 98.5%, and no sero-reversion, or symptomatic COVID-19. Studies assessing the humoral response after a two-dose regimen in dialysis patients showed a sero-reversion rate of 5.8% at 3 months [7] and 32% at 6 months [8]. This confirms the need for a three-dose regimen and further suggests that a fourth boost dose should be considered in this population to increase both breadth and cross-reactivity of neutralizing antibodies, given the potential of the SARS-CoV-2 to escape vaccine-induced humoral response [9].

Study limitations include small sample size, a limited follow-up of 6 months, and lack of cellular immunity testing and neutralizing antibody testing.

To conclude, our results show that after a three-dose regimen of the BNT162b2 vaccine, antibody titer decreased over time with a significant number of dialysis patients with a low antibody titer, even if no sero-reversion or symptomatic COVID-19 occurred at 6 months. Given the pandemic’s ongoing waves of new infections, a fourth boost dose should be proposed to obtain a sustained protective humoral response in this population.

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Data availability The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Conflict of interest None.

Disclosures None.

Ethics approval and informed consent According to French law (Loi Jardé), anonymous retrospective studies do not require institutional review board approval.

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