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RESEARCH LETTER

Humoral immunity against Covid-19 six months after the Pfizer BNT162b2 vaccine in hemodialysis patients: data from five dialysis units. Is there a protective role for hemodiafiltration in the Covid-19 pandemic?

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Global vaccination against SARS-CoV2 began in 2021, but only a small proportion of patients with renal disease have been included in clinical trials, and long-term data on dialysis patients are still scant. These immunocompromised patients also have a poorer response to other vaccines [1], hence it is important to understand if there is a need for a tailored immunization protocol against SARS-CoV2.

We therefore studied the immune responses after the first two doses of the Pfizer BNT162b2 vaccine in hemodialysis (HD) patients for 6 months.

We conducted an observational, prospective, multicenter study in five BBRAUN renal care units between January 25, 2021, and August 31, 2021. Adult HD patients in the five clinics received two shots of the Pfizer BNT162b2 vaccine, 21 days apart. Blood was drawn at the beginning of dialysis to measure seroconversion responses 21 days after the first dose (D22), 21 days after the second dose (D43), and 3 and 6 months after the first dose (M3 and M6, respectively).

Serologic tests were run using an Abbott chemiluminescent microparticle immunoassay. The percentage of responders and quantitative antibody levels were assessed during the 6 months following vaccination, as were the incidence of SARS-CoV2 infection, hospitalization, and death.

Continuous variables are presented as means, standard deviations or quartiles. Categorical variables are presented as frequencies. Wilcoxon nonparametric test and Kruskal–Wallis test were used to compare paired and independent observations, respectively. Chi-square test or Fisher's exact test were used to test associations. Bonferroni method was used to adjust significance levels. Predictors of positivity and predictors of antibody levels were determined by logistic and linear regression models, respectively. In the first case, linearity of logit was tested. In the second case, multicollinearity was analyzed. A statistical significance of $p < 0.05$ was considered.

A total of 404 patients were included in the study. Sixty point six percent were male, and median age was 70 years. Twenty-six patients (6.4%) had previously been infected with Covid-19. Six of them needed hospitalization, and none died from the disease. After 6 months, there were three new infections. Two of them needed hospitalization and one died.

The maximum response to the vaccine was seen at D43 (97.3% antibody positivity). At 6 months, 91.5% still had positive antibodies. Between D43 and M6, there was a significant median drop of 85% in antibody levels ($p < 0.001$). The greatest variation between two consecutive blood samples was seen between M3 and M6 (median drop of 69%; $p < 0.001$).

Comorbidities, such as obesity, hypertension, diabetes, and chronic respiratory failure, did not affect the serologic response, nor did the gender, cause of renal failure, type of vascular access, history of kidney transplant, or dose of dialysis. Other variables, such as normalized protein catabolic rate, hemoglobin, leukocyte count, alanine transaminase, C-reactive protein, or the Charlson Comorbidity Index, did not impact the immunological response.

Independent predictors of higher antibody levels at D43 and M6 were, respectively: patients with previous infection (B 2.492 [95% CI 1.794; 3.190]; B 3.097 [95% CI 2.429;

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3.765]), younger patients (B 0.023 [95% CI 0.033; 0.013]; B 0.019 [95% CI 0.029; 0.010]), patients on hemodiafiltration (HDF) vs. HD (B 0.534 [95% CI 0.208; 0.859]; B 0.493 [95% CI 0.187; 0.799]), and patients with higher albumin levels (B 0.717 [0.267; 1.167]; B 0.708 [0.290; 1.125]).

HDF was significantly associated with higher antibody levels at all time points, as shown in Fig. 1, when compared to HD.

Concerning antibody positivity, logistic regression showed that patients with cancer without antineoplasic treatment in the previous 6 months showed lower rates of seroconversion at D43 (OR 0.117 [95% CI 0.016; 0.863]) and M6 (OR 0.203 [95% CI 0.049; 0.842]). Patients whose levels of C-reactive protein were ≤ 2.8 mg/dL had more probability of seroconversion at D43 (OR 7.840 [95% CI 1.839; 33.419]) as did those with a higher (better) Karnofsky score (OR 1.062 [95% CI 1.016; 1.110]). Patients < 60 years showed a higher probability of seroconversion at M6 (OR 11.316 [95% CI 1.493; 5.759]).

Further results are available as supplemental data.

The data available in the literature mostly reported early response to vaccination [2–4], but the durability and persistence of vaccine-induced immunity in HD patients is still mostly unknown. A clinically relevant finding of our study is that, despite a significant drop in antibody titers at 6 months, 91.5% of our patients still had positive antibodies, suggesting a sustained response over time.

An unexpected result of our study was the consistent link found between HDF and higher antibody levels, when compared to HD. We tried to adjust for possible confounders, such as age, functional status, albumin, C-reactive protein, and others, but the tendency remained clear. This observation might have practical implications during the pandemic. One possible explanation may be related to previous studies suggesting that HDF may reduce inflammation [5], which could, in turn, contribute to a stronger immune response.

In conclusion, our data show that patients on HDF respond surprisingly well to anti-Covid-19 vaccination. A possible strategy in dialysis patients might be to regularly measure anti-SARS-CoV2 antibody titers to identify the patients' needs and determine whether booster doses are required.

Further studies should analyze the impact of HDF on immune responses, since our work suggests it may have positive, long-term protective effects in our dialysis population.

Additional large studies are needed to assess the extent of protection after vaccination and whether detectable levels of immunogenicity translate into real clinical protection, as suggested by our analysis regarding Covid-19 infection.

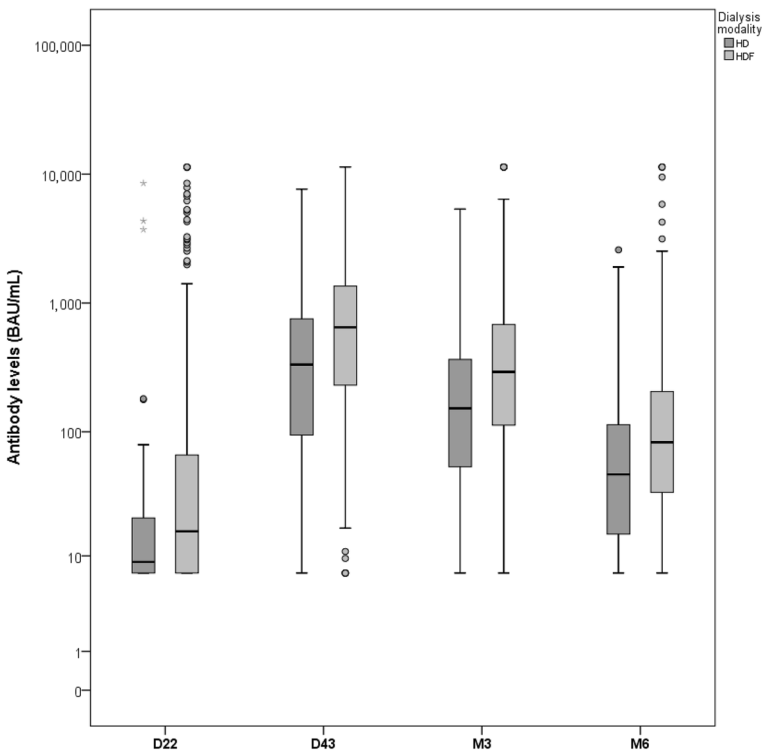

Fig. 1 Antibody levels in patients on HD vs. HDF

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40620-022-01350-9.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Ethical statement Nothing to declare.

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