Clinical Kidney Journal

Clinical Kidney Journal, 2022, vol. 15, no. 8, 1633–1635

https://doi.org/10.1093/ckj/sfac148
Advance Access Publication Date: 24 May 2022
Letter to the Editor

LETTER TO THE EDITOR

Humoral response after SARS-CoV-2 booster vaccination in haemodialysis patients with and without prior infection

Louise Füessl[1], Tobias Lau[2], Simon Rau[2], Ron Regenauer[1], Michael Paal[3], Sandra Hasmann[1], Florian M. Arend[3], Mathias Bruegel[3], Daniel Teupser[3], Michael Fischereder [1,*] and Ulf Schönermarck [1,*]

[1]Department of Medicine IV, University Hospital of Munich, Munich, Germany, [2]Dialysezentrum Bad Tölz und Wolfratshausen, Bad Tölz, Germany and [3]Institute of Laboratory Medicine, University Hospital of Munich, Munich, Germany

*These authors contributed equally to this work.
Correspondence to: Ulf Schönermarck; E-mail: Ulf.Schoenermarck@med.uni-muenchen.de

Vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) proved to prevent severe coronavirus disease 2019 (COVID-19) infection among dialysis patients, who represent a particularly vulnerable population with a high rate of morbidity and mortality. Several cohorts, including our own, showed a favourable, albeit diminished, early antibody response with declining antibody titres within 6 months of vaccination [1–4].

It has been demonstrated that a booster vaccination can restore and also increase the waning antibody response in the general population [5]. These observations could be confirmed in dialysis patients [3, 6–9]. However, data on the humoral antibody response after a first and second booster are still scarce [9, 10].

We retrospectively analysed 100 haemodialysis (HD) patients who received one or two booster vaccinations with an messenger RNA vaccine after complete COVID-19 vaccination according to national recommendations.

The first booster was administered at a median of 7 months after a complete course of COVID-19 vaccination ($n = 100$). The second booster was administered at a median of 5 months after the first booster ($n = 83$). Anti-SARS-CoV-2 spike (S) antibody measurements are shown in Fig. 1 and patients' characteristics in Supplementary data, Table S1.

Anti-SARS-CoV-2 S antibody levels significantly increased after the first booster vaccination from 95.3 U/mL [interquartile range (IQR) 27.0–232.5) (M1) to 14 769.5 U/mL (IQR 6374.7–25 001) (M2, $P < .001$) in uninfected patients and from 3581 U/mL (IQR 1288.5–11 660) to 40 380 U/mL (IQR 22 128; 127 500) ($P < .001$) in patients with previous infection (Fig. 2). After a median time of 4.9 months, anti-SARS-CoV-2 S antibody levels significantly declined in uninfected patients to 3894 U/mL (IQR 1579–9446), (M3, $P < .001$) and previously infected patients to 23 456 U/mL (IQR 7799–65 090), ($P < .001$).

Following the second booster, anti-SARS-CoV-2 S antibody titres significantly increased in uninfected patients to 21 633 U/mL (IQR 11 369–64 660), (M4, $P < .001$) as well as in patients with prior infection to 46 470 U/mL (IQR 19 423–1110 000), $P < .001$) and exceeded antibody levels after the first booster. Antibody levels were significantly higher before and after the first booster, as well as before the second booster vaccination in infected patients compared with uninfected patients ($P < .001$). However, anti-SARS-CoV-2 S antibody titres in uninfected patients approximated those of infected subjects after the second booster without a significant difference between both groups at M4.

In a multivariate regression analysis, previous COVID-19 infection was associated with higher antibody response only after the first booster vaccination ($P = .001$). A significant inverse

Received: 17.5.2022; Editorial decision: 19.5.2022

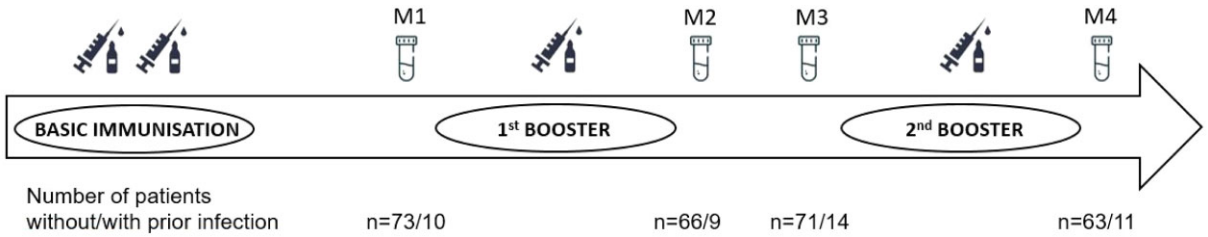

FIGURE 1: Timeline of vaccination and antibody measurement. The first booster vaccination was applied at a median of 7.4 months after full COVID-19 vaccination. The second booster was applied 4.9 months after the first booster vaccination. Anti-SARS-CoV-2 S antibody titres were assessed (M1) before the first booster vaccination (corresponding to a median of 7.4 months after full COVID-19 vaccination), (M2) 4 weeks after the first booster vaccination, (M3) before the second booster vaccination (corresponding to a median of 4.9 months after full COVID-19 vaccination) and (M4) 4 weeks after the second booster vaccination. Depicted are the number of patients for measurement and the distribution of patients with and without prior COVID-19 infection at the given time points.

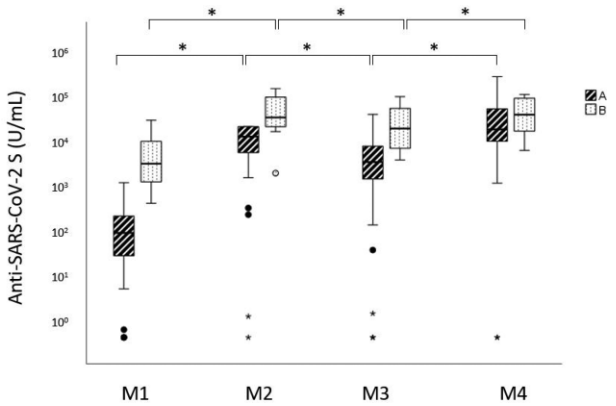

FIGURE 2: Anti-SARS-CoV-2 S antibody response in HD patients after first and second COVID-19 booster vaccination. Anti-SARS-CoV-2 S antibody titres are shown in HD patients after full COVID-19 vaccination either (**A**) uninfected or (**B**) with prior COVID-19 infection: (M1) before the first booster vaccination (corresponding to a median of 7.4 months after full COVID-19 vaccination), (M2) 4 weeks after the first booster vaccination, (M3) before the second booster vaccination (corresponding to a median of 4.9 months after full COVID-19 vaccination) and (M4) 4 weeks after the second booster vaccination. The box shows the IQR, the horizontal line inside the box represents the median values and whiskers represent the minimum and maximum range of points within 1.5 times the IQR in the box. *$P < .001$

correlation with the use of systemic immunosuppression at both points of time ($P < .001$) could be observed (Supplementary data, Table S2).

Our data agree with current studies showing a good antibody response in HD patients after a booster vaccination [3, 6, 7, 9, 10]. This is in line with other successful strategies in HD patients (e.g. hepatitis B) using higher or multiple vaccine doses. Only two studies have reported results of two booster vaccinations [9, 10], albeit with a smaller sample size, exclusion of infected patients or application of the first three doses within a short time frame.

Furthermore, these findings confirm that vaccinated HD patients with a previous COVID-19 infection have a higher or at least comparable antibody titre compared with uninfected boosted patients [7]. For these patients, the need for further booster vaccinations might be postponed.

We acknowledge the limitations of our study: the small sample size, the lack of assessment of the cellular response and exclusion of patients without booster vaccination. However, in contrast with other studies excluding patients with prior COVID-19 infection or immunosuppression, this approach displays the real-life situation within a dialysis unit.

In conclusion, a first COVID-19 booster significantly increases the antibody response in HD patients. The following decline in antibody titres can be successfully reversed with a second booster. Patients with prior COVID-19 infection elicit significantly higher antibody responses. This argues in favour of regular booster vaccinations and suggests that regular assessment of quantitative antibody titres is useful. Further studies should establish protective thresholds and determine when booster vaccinations are of most clinical benefit.

SUPPLEMENTARY DATA

Supplementary data are available at *ckj* online.

ACKNOWLEDGEMENTS

We thank all patients for their participation in the study. We also thank the staff of the dialysis centres for their excellent assistance. The study was approved by the local institutional review board of the University Hospital of Munich (21–1226).

CONFLICT OF INTEREST STATEMENT

The authors have no competing interests to declare that are relevant to the content of this work.

AUTHORS' CONTRIBUTIONS

M.F. and U.S. were responsible for conceptualization. U.S. and L.F. were responsible for the methodology. L.F., T.L. and U.S. were responsible for formal analysis and draft preparation. All authors were responsible for resources and review and editing of the manuscript. L.F. and S.H. were responsible for visualization. U.S. and M.F. were responsible for supervision. All authors have read and agreed to the published version of the work.

FUNDING

This research received no external funding.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study will be shared upon reasonable request to the corresponding author.

REFERENCES

1. Davidovic T, Schimpf J, Abbassi-Nik A *et al*. Waning humoral response 6 months after SARS-CoV-2 vaccination with the mRNA-BNT162b2 vaccine in hemodialysis patients: time for a boost. *Kidney Int* 2021; **100**: 1334–1335
2. Füessl L, Lau T, Lean I *et al*. Diminished short- and long-term antibody response after SARS-CoV-2 vaccination in hemodialysis patients. *Vaccines* 2022; **10**: 605
3. Hsu CM, Lacson EK, Manley HJ *et al*. Seroresponse to third doses of SARS-CoV-2 vaccine among patients receiving maintenance dialysis. *Am J Kidney Dis* 2022; doi: 10.1053/j.ajkd.2022.03.002
4. Paal M, Arend FM, Lau T *et al*. Antibody response to mRNA SARS-CoV-2 vaccines in haemodialysis patients. *Clin Kidney J* 2021; **14**: 2234–2238
5. Magen O, Waxman JG, Makov-Assif M *et al*. Fourth dose of BNT162b2 mRNA Covid-19 vaccine in a nationwide setting. *N Engl J Med* 2022; **386**: 1603–1614
6. Benning L, Klein K, Morath C *et al*. Neutralizing antibody activity against the B.1.617.2 (delta) variant before and after a third BNT162b2 vaccine dose in hemodialysis patients. *Front Immunol* 2022; **13**: 840136
7. Biedunkiewicz B, Tylicki L, Ślizień W *et al*. Waning humoral response after COVID-19 mRNA vaccination in maintenance dialysis patients and recovery after a complementary third dose. *Vaccines* 2022; **10**: 433
8. Broseta JJ, Rodríguez-Espinosa D, Cuadrado E *et al*. Humoral response after three doses of mRNA-1273 or BNT162b2 SARS-CoV-2 vaccines in hemodialysis patients. *Vaccines* 2022; **10**: 522
9. Housset P, Kubab S, Hanafi L *et al*. Humoral response after a fourth "booster" dose of a coronavirus disease 2019 vaccine following a 3-dose regimen of mRNA-based vaccination in dialysis patients. *Kidney Int* 2022; **101**: 1289–1290
10. Cinkilic O, Anft M, Blazquez-Navarro A *et al*. Inferior humoral and sustained cellular immunity against wild-type and omicron variant of concern in hemodialysis patients immunized with 3 SARS-CoV-2 vaccine doses compared with 4 doses. *Kidney Int* 2022; **101**: 1287–1289