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Letter to the Editor

LETTER TO THE EDITOR

Heterogeneous neutralizing antibodies production after SARS-CoV-2 vaccination in haemodialysis patients

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination is the key point in the fight against the current pandemic. Haemodialysis patients are at particularly high risk of severe disease and death due to their comorbidities and their acquired immunodeficiency [1]. Unfortunately, it has been shown that neutralizing antibodies (NAbs) production after vaccination is impaired in haemodialysis patients compared with healthy patients [2]. Indeed, uraemia inhibits antibody production, as has been shown with other vaccines such as hepatitis B or influenza [3]. Currently, the vaccination strategy in haemodialysis patients consists of three doses in patients never infected by SARS-CoV-2, and two doses of vaccine in patients previously infected.

Protection after SARS-CoV-2 vaccination or infection is difficult to establish [4]. Indeed, immune status may be determined by routine serological tests that usually detect antibodies against spike protein (S) and/or nucleoprotein (N). However, most of these currently available tests fail to ascertain the neutralizing activity of the antibodies detected. In order to identify patients who would benefit from extra vaccine boosts, a more specific test is needed to assess SARS-CoV-2 NAbs positivity and to establish a reliable correlation with usual serological tests.

We aimed to analyse the neutralizing activity of sera of patients with a surrogate virus neutralization test (iFlash-2019-nCoV Nab assay, Ylho, China) and compared results versus total anti-SARS-CoV-2 titre (TAb, corresponding to both neutralizing and non-neutralizing anti-S antibodies; Elecsys, Roche Diagnostics, Meylan, France) in two sets of samples:

- Samples collected 4 weeks after the second dose and 4 weeks after the third dose in naïve patients for SARS-CoV-2;
- Samples collected 4 weeks after the first dose and 4 weeks after the second dose in patients previously exposed to SARS-CoV-2.

The protective cut-off for NAbs was defined as >24 UI/mL, whereas positive serology for TAb was defined as >0.8 UI/mL.

In naïve patients, 4/7 patients reached the protective cut-off for NAbs after two doses (mean 129 UI/mL, median 125 UI/mL) and 6/7 patients after the third dose (mean 1349 UI/mL, median 1911 UI/mL). This was associated with a similar induction of TAb with positivity in 5/7 patients after two injections (mean 121 UI/mL) and 6/7 patients after three doses (mean 192 UI/mL).

In previously infected patients, NAbs median was 110 UI/mL 4 weeks after the first dose and lowered, at 87 UI/mL, 4 weeks after the second dose. Both levels were lower than those observed

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in naïve patients. All previously infected patients (4/4) presented positive TAb after the first and after the second injection, but levels were higher after the second injection (mean 130 UI/mL) compared with the first injection (mean 80 UI/mL).

Our results highlight the possible negative impact of a previous SARS-CoV-2 infection on development of an efficient immune response after vaccination in haemodialysis patients. Indeed, NAbs measures in previously infected patients show a lower production 4 weeks after the second injection compared with 4 weeks after the first injection, while these rates increase after the third injection in naïve patients. These results contrast with routine tests, based on TAb titres, which indicate higher rates 4 weeks after the third injection in naïve patients and after the second injection in previously infected patients. A limitation of the present data is the lack of exploration of cell-mediated immunity.

To conclude, the level of protection after SARS-CoV-2 vaccination is heterogeneous in haemodialysis patients, with some of them being protected after two injections whereas others show poor protection after three injections. Previous SARS-CoV-2 infection could modulate this response. In this particular population, with easy access to blood tests and NAbs assays, the number of injections necessary could be based on the monitoring of NAbs titres.

CONFLICT OF INTEREST STATEMENT

None declared.

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