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Optimal Timing of COVID-19 Vaccination in the Peri-Transplant Period: A Single Institution Case Series

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ABSTRACT

The outcomes of vaccination against Severe Acute Respiratory Syndrome Coronavirus 2 in organ transplant recipients are unclear. Recent studies have investigated outcomes for patients who are several years post transplant. There has not been much data in peri-transplant patients. This is important because patients are highly immunosuppressed during this period owing to induction immunosuppression and are thus susceptible to infection. We looked at 6 patients who were transplanted at our center after receiving their first dose of mRNA vaccines. We assessed their antibody response after 1, 2, and in two patients, 3 doses of the vaccine. Out of the two patients who received their third booster dose, one had a detectable antibody level after the third dose. We report that the overall antibody response to vaccination was weaker in transplant patients compared with the general population, with a rapid attrition of antibody response over time. There is a need for more studies that follow-up antibody levels in transplant patients over time, especially those in the peri-transplant period to help guide the vaccination plan for immunosuppressed transplant patients.

DATA AVAILABILITY

Data will be made available on request.

Vaccination against SARS-CoV-2 with mRNA-1273 (Moderna) and BNT162b2 (Pfizer-BioNTech) vaccines has been noted to be highly effective in the general population [1,2]. However, the outcomes in immunocompromised transplant recipients are unclear from the original studies because these individuals were excluded from those studies. There has been a recent report to assess the immunogenicity of a single dose of the mRNA vaccines in solid organ transplant recipients [3]. The authors reported that only 17% of patients had a detectable antibody response after a single dose of the mRNA vaccine. More recently, the same group reported the outcomes after both doses of vaccine. Antibody was detectable in 54% of the patients after the second dose [4]. Compared to this, the antibody response in dialysis patients has been reported to be better, with 90% to 96% patients with detectable antibody after both doses of the vaccine, albeit with a much lower antibody titer compared with the general population [5,6]. The median time since transplant for these patients was 6.2 years. There is still no data about vaccine efficacy in the peri-transplant period.

Many unanswered questions remain when a kidney becomes available for a waitlisted patient:

- Should patients receive both doses of vaccine before transplantation (and be inactive on the waitlist during that time)?
- How long should patients wait before activation on the waitlist after completing vaccination?
- If not vaccinated pretransplant or if receiving only 1 dose before transplantation, how long should patients wait after transplantation to get vaccinated?
- Should patients receive a booster dose of the vaccine? If yes, what’s the ideal time interval between the second dose and booster dose?

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MATERIALS AND METHODS

Herein, we report our single institution experience with 6 patients who underwent kidney transplantation after having received a single dose of mRNA vaccine (Pfizer-BioNTech-4 patients, Moderna-2 patients) at a median of 12.5 days (8-23 days) before transplant (Table 1). Median age of recipients was 62.5 years (53-79 years). All patients received alemtuzumab (Campath) induction and maintenance immunosuppression with tacrolimus ER (Envarsus) and mycophenolate sodium (Myfortic). Three patients had rapid steroid taper, and 3 patients were maintained on low-dose prednisone as per our institutional protocol. All patients had uneventful postoperative course and primary graft function. None of the patients have had COVID-19 infection pretransplant or posttransplant. No patient developed acute rejection after vaccination.

During follow-up, we tested the patients using an enzyme immunoassay (EUROIMMUN SARS-CoV-2 ELISA) for detection of IgG antibodies against the spike protein (S1) of SARS-CoV-2 a median of 44.5 days (19-48 days) after vaccination. Per laboratory protocol, a reference interval index of $<0.7$ was a negative test, $>1.1$ index was considered positive, and an index of 0.8 to 1.0 was considered indeterminate.

RESULTS

After the first dose, 4 patients had negative antibody tests, and 2 patients had detectable anti–spike protein IgG antibodies. After the second dose, 2 patients had detectable antibodies, 3 patients were negative, and one was indeterminate owing to low titer of antibodies.

Interestingly, 2 patients (patients 5 and 6) who had detectable antibodies after the first vaccine dose had undetectable antibodies after the second dose, whereas 2 patients who had undetectable antibodies after the first dose had detectable antibodies after the second dose. One patient (patient 2) continued to have no detectable antibodies after the second dose and more recently after the third (booster) dose as well. Another patient (patient 3) had indeterminate levels of antibodies (index - 0.9) after the second dose but became positive after a third booster dose of the vaccine. None of the patients contracted COVID-19 infection before or after transplant.

DISCUSSION

Although this is a small, single-center, case series, we did find that the antibody response to the first dose in these patients was weak with only 2 out of 6 patients with detectable antibody levels. Both these patients with positive antibody response got their test within 30 days of receiving the vaccine. Other patients who had their antibody levels checked more than 30 days after getting their first shot had undetectable antibody levels. This is likely attributable to the rapid attrition of antibodies in immunosuppressed transplant patients, which is much quicker than in the general population [7,8].

We also found in this small series that patients receiving Moderna vaccine had more likelihood of having detectable antibody levels after 2 doses than patients receiving the Pfizer-BioNTech vaccine.

Two patients (patient 2 and 3), both without adequate detectable antibody response after the first 2 vaccine doses, received a
third booster dose. Although patient 3 was able to mount an antibody response after that, patient 2 continued to have undetectable antibody levels even after the booster dose.

Given the results of this study and the data on immunogenicity of vaccines posttransplant [3,4], and in dialysis patients [5,6], we recommend fully vaccinating patients before activating on the waitlist and placing the waitlisted kidney transplant patients on hold until they receive both doses of the vaccine, as recommended by American Society of Transplantation [9].

In case a patient is transplanted after a single mRNA vaccine dose, we suggest waiting for at least 6 weeks, getting a second dose of the vaccine, followed by a third booster dose after at least 6 weeks [10] and then testing for the presence of anti–spike protein IgG antibodies after that to determine if additional vaccine doses are warranted. A fourth dose of the vaccine is not currently approved by the FDA. It is also uncertain if the patients not responding to the first 3 doses of the vaccine will respond to a fourth dose, even though there has been a recent small case series showing that 5 out of 8 (63%) patients with negative to low positive titers showed boosting to high-positive titers after a fourth dose of the vaccine [11]. Patients who do not develop an antibody response after 3 doses should be extra-cautious knowing that they are not well protected against future SARS-CoV-2 infection and morbidity/mortality because of the infection [12,13]. These patients can be considered for early monoclonal antibody treatment to reduce their chances of getting a serious infection as reported in this single institution case series [14]. It would also be prudent for the caregivers of these patients to be vaccinated to prevent infection. There are currently no guidelines for patients who continue to have undetectable antibody levels after the booster dose.

More studies are needed to assess the antibody and cellular responses of immunosuppressed transplant patients to vaccination in the peri-transplant period. These studies should sequentially monitor the antibody responses over time to look for attrition of antibody response, which is expected to be quicker in this population.

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