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Protecting kidney transplant recipients against SARS-CoV-2 infection: A third dose of vaccine is necessary now

To the Editor:

We have read the article written by Ison et al.[1] that has raised some issues we would like to discuss. COVID-19 breakthrough infection rates in vaccinated kidney transplant (KT) recipients much higher than in the general vaccinated population have been reported.[2] Furthermore, the severity remains markedly high. Although Ison et al. referred cases are rarely severe, other series, and among them, the largest cohort published so far, have reported 27% of very serious cases.[3]

By August 2021, 843 KT recipients at our center have been fully vaccinated against COVID-19. During this period, 15 patients developed COVID-19 after two doses of mRNA-based vaccines: 1.8% versus 0.01% in the general population.[2] Of them, five needed hospitalization (33.3%): three remain in critical care units and one died. Contrary to what Ison et al. stated, also in our experience, severe COVID-19 has not been uncommon in infected vaccinated KT patients.

TABLE 1 Factors associated with response to mRNA-based vaccines

	Total ($n = 91$)	Seroconversion ($n = 57$)	No seroconversion ($n = 34$)	*p*
Vaccine type, *n* (mRNA-1273/BNT162b2)	84/7	56/1	28/6	
Antibody titer U/ml, median [IQR]	20.5 [1.5–95]	63.9 [27.1–268.7]	0.72 [0.2–2.8]	<.001
Male gender, *n* (%)	61 (67)	42 (73.7)	19 (55.9)	.091
Age, median [IQR]	59 [51–66]	59 [50–64.5]	62.5 [58–70.5]	.022
Age ≥65 years, *n* (%)[a]	30 (33)	14 (46.7)	16 (53.3)	.027
Time from KT to COVID-19 vaccine (months), median [IQR]	64 [22–158]	96 [41–187]	27.5 [17.5–110.7]	.004
Thymoglobulin, *n* (%)[b]	5 (5.5)	2 (3.5)	3 (8.8)	.282
Rituximab[b]	1 (1.1)	0	1 (2.9)	.193
Prednisone, *n* (%)	87 (95.6)	53 (93)	34 (100)	.114
Tacrolimus, *n* (%)	84 (92.3)	51 (89.5)	33 (97.1)	.189
MPA, *n* (%)	76 (83.5)	44 (77.2)	32 (94.1)	.035
mTOR inhibitors, *n* (%)	10 (11)	8 (14)	2 (5.9)	.229
Azathioprine, *n* (%)	2 (2.2)	1 (1.8)	1 (2.9)	.709
AR episode, *n* (%)[b]	3 (3.5)	2 (3.6)	1 (3.2)	.921
Serum creatinine, median [IQR]	1.3 [1.1–1.6]	1.2 [0.9–1.5]	1.4 [1.3–1.8]	.002
Multiple logistic regression analysis for seroconversion				
		OR (95% CI)		***p***
Recipient age		0.94 (0.89–0.99)		.024
Time from KT to COVID-19 vaccine		1.00 (1.00–1.01)		.011
Serum creatinine		0.28 (0.12–0.68)		.005
MPA		0.08 (0.01–0.53)		.008

Abbreviations: CI, confidence interval; IQR, interquartile range; MPA, mycophenolic acid; OR, odds ratio.

[a]Percentage within age < or ≥65 years.

[b]In the last year prior to COVID-19 vaccine.

Although serological protective thresholds are not established yet, higher antibodies titers are associated with a less severe COVID-19 in the general population.[4] We analyzed the response after two doses of mRNA-based vaccine in 97 randomly selected stable KT recipients (Abbott SARS-CoV-2 IgG chemiluminescent microparticle immunoassay). Six patients had COVID-19 previously; they all had detectable antibodies prior to vaccination, with a 20-fold increase 1 month after the second dose (201.8 vs. 3601.2 U/ml; $p = .005$). The rest of the patients were seronegative before the vaccine; in this group, the seroconversion rate was 62.6% 1 month after two vaccine doses. A shorter post-KT time, renal function, treatment with mycophenolic acid (MPA) and age were related to a lower response (Table 1). These last two factors have already been identified for a weak immune response.[5] Thus, temporary withdrawal of MPA during the vaccination could be a strategy to increase the serological response in selected patients, although this needs to be carefully analyzed.

As in other series, these results have aroused interest in the administration of a booster dose in KT. The early data showed that, after this third dose, the seroconversion rate increased about 20% and there were no breakthrough infections during the follow-up.[1,5] Recently the Food and Drug Administration approved a third dose in immunocompromised population but most European countries, including Spain, have not yet made a decision.

Ison et al. presented their concern about the potential risk of acute rejection (AR) after the third dose of the vaccine. Notwithstanding, only one case has been reported,[1] so it is difficult to establish a causal association. The French study, with 396 solid organ transplant patients who received the third dose, did not observe any AR episode.[5]

In conclusion, we think that vaccination programs with a third dose should be fostered in KT recipients as long as we do not have more effective treatments or vaccines. A booster dose increases the response and it is unlikely to be associated with AR. Changes in immunosuppressive therapy could perhaps be proposed in some patients to improve the response to vaccine.

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basic (laboratory) research/science, clinical research/practice, infectious disease, kidney transplantation/nephrology, patient safety, patient survival, vaccine

DISCLOSURE

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