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Serological response to mRNA SARS-CoV-2 BNT162b2 vaccine in kidney transplant recipients depends on prior exposure to SARS-CoV-2

To the Editor:

Grupper et al. have reported on a positive humoral response *post* full vaccination with mRNA SARS-CoV2 BNT162b2 in only 51/136 (37.5%) kidney transplant recipients (KTRs) without prior exposure to the virus.[1] We have conducted an IRB-approved (B707201215598–2021/80) prospective small sample-size study comparing the humoral response to BNT162b2 in 40 consecutive individuals early exposed to the Belgian vaccination program, including 20 KTRs with (*n* = 10, COVID-19(+)) vs. without (*n* = 10, COVID-19(–)) history of exposure to SARS-CoV-2 and 20 controls including 10 COVID-19(+) vs. 10 COVID-19(–). The quantification of S1/S2 IgGs by DiaSorin LIAISON® chemiluminescence immunoassay was performed at three time-points: first BNT162b2 injection (T1); second BNT162b2 injection (T2, i.e., ~21 days *post* T1); and ~15 days after T2 (T3). The generalized linear mixed model tested the effects of time, group, and interactions. No epidemiological difference was observed between KTRs vs. controls, nor between COVID-19(+) vs. COVID-19(–) (Table 1). The median delay between PCR-proven COVID-19 and T1 was 129 [64; 352] days. None of the 20 KTRs received IV corticosteroids or rituximab within 12 months prior to vaccination.

At T1, the median concentration of S1/S2 IgGs in the 20 COVID-19(+) was 56 [0; 205] AU/ml. No IgG was detectable in COVID-19(–) individuals (Table 1). At T2, a response was observed in 19/20 controls, with significantly higher IgG titers in COVID-19(+) compared to COVID-19(–). In KTRs, no humoral response was observed in COVID-19(–) whereas all COVID-19(+) showed detectable IgG levels. The magnitude of serological response was not different between COVID-19(+) KTRs and COVID-19(+) controls (Table 1). At T3, all controls had measurable IgGs, with significantly higher titers in COVID-19(+) vs. COVID-19(–). In KTRs, IgGs were detectable in only 1/10 COVID-19(–) (60 AU/ml), whereas IgG levels in COVID-19(+) KTRs were similar to COVID-19(+) controls (Table 1). An additional serological testing of the 10 COVID-19(–) KTRs after 50 days [39; 121] *post* T2 was positive in 3/10, with median IgG titers of 30 AU/ml [15; 46]. From a longitudinal point of view, serum S1/S2 IgG levels in the 20 COVID-19(+) KTR and non-KTR individuals increased significantly from T1 to T2, with no further increase from T2 to T3. The kinetics was different in the 10 COVID-19(–) controls, with significant increases from T1 to T2 and from T2 to T3.

As a whole, a history of COVID-19 impacts the kinetics and the magnitude of S1/S2 IgG development ***post*** BNT162b2 vaccination in KTRs, as recently demonstrated by Cucchiari et al.[2] We have no information about the cellular response ***post*** BNT162b2 vaccination in our cohort. Consistently with recent publications, SARS-CoV-2-naïve KTRs have a poor serological response to BNT162b2 vaccine.[1,3,4] One may not exclude that additional vaccine injections and/or a longer follow-up may eventually elicit a full humoral response in KTRs. Still, given the current knowledge, KTRs with no history of PCR-proven COVID-19 should be advised to maintain the WHO sanitary recommendations[5] against SARS-CoV-2 after BNT162b2-based vaccination. By contrast, one single BNT162b2 injection might be sufficient in KTRs with detectable S1/S2 IgGs before vaccination.

KEYWORDS

clinical research/practice, immunosuppressant, immunosuppression/immune modulation, infection and infectious agents – viral, infectious disease, kidney transplantation/nephrology, vaccine

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TABLE 1 Characteristics of the cohort

Parameters	Controls *n* = 20		Kidney transplant recipients *n* = 20		
	COVID−19 (−) *n* = 10	COVID−19 (+) *n* = 10	COVID−19 (−) *n* = 10	COVID−19 (+) *n* = 10	*p* value
Age, years	51.5 (10.5)	45.1 (10.4)	49.7 (13.8)	52.7 (13.8)	0.53
Female gender, n (%)	3 (30)	4 (40)	5 (50)	6 (60)	0.57
BMI, kg/m^2	24.58 (3.28)	25.68 (2.95)	26.45 (3.84)	26.45 (4.67)	0.71
Time from KTx, months			121.7 (106.0)	77.8 (41.8)	0.57
Deceased donor, n (%)			8 (80)	9 (90)	0.53
CNIs, n (%)			10 (100)	10 (100)	1.00
Antimetabolite, n (%)			10 (100)	7 (70)	0.37
mTOR inhibitors, n (%)			0 (0)	1 (10)	1.00
Methylprednisolone, n (%)			4 (40)	5 (50)	1.00
Serum creatinine, mg/dl			1.08 (0.29)	1.55 (0.61)	0.13
Delay between COVID-19 and vaccination, days		154.2 (107.1)		158.2 (77.0)	0.44
Evolution of anti-S1/S2 IgG titer					
T1, median (min–max), AU/ml = first BNT162b2 injection	0 (0)	35 (0–98)	0 (0)	107 (0–205)	<0.001[a] <0.001[b] 0.031[c] 1.00[d]
T2, median (min–max), AU/ml = second BNT162b2 injection	35.5 (0–118)	1520 (79–7290)	0 (0)	1131 (94–9040)	<0.001[a] <0.001[b] 0.59[c] <0.001[d]
T3, median (min–max), AU/ml = ~15 days after T2	263 (153–2090)	2300 (1470–6250)	0 (0–60)	2105 (212–18300)	<0.001[a] <0.001[b] 0.88[c] <0.001[d]
T4, median (min–max), AU/ml = ~50 days after T2			0 (0–46)		

Note: Data presented as mean (SD) unless otherwise stated.

Abbreviations: AZA, azathioprine; BMI, body mass index; CNIs, calcineurin inhibitors; KTx, kidney transplantation; MMF, mycophenolate mofetil; MPA, mycophenolate sodium; mTORs, mammalian target of rapamycin inhibitors.

[a]KTR COVID-19(+) vs. KTR COVID-19(−).

[b]Control COVID-19(+) vs. control COVID-19(−).

[c]KTR COVID-19(+) vs. control COVID-10(+).

[d]KTR COVID-19(−) vs. control COVID-19(−).

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