Neutralization of B.1.617.2 variant through antibodies elicited by ChAdOx1-S, BBIBP-CorV, and Gam-COVID-Vac in an Argentinean cohort

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RESUMEN

There is global increasing concern about the emergence of SARS-CoV-2 variants along with a decrease of vaccine effectiveness. The role of humoral response in the efficacy of vaccines against variants has focused on antibodies that neutralize SARS-CoV-2, since neutralization strongly correlates with protection from symptomatic infection. 1 We report our evaluation of the neutralizing potential of antibodies (NPA) elicited by natural infection and/or vaccination against SARS-CoV-2 B.1.617.2 variant, compared to the ancestral wild-type (WT) virus lineage B.1. We studied 309 plasma samples from individuals sorted into four groups: (1) Unvaccinated and recovered from infection by ancestral WT-B.1 (n = 41); (2) vaccinated with two doses of ChAdOx1-S (n = 78); 21 had SARS-CoV-2 infection prior to vaccination (IPV); (3) vaccinated with two doses of BBIBP-CorV (n = 101); 40 with IPV; (4) vaccinated with two doses of Gam-COVID-Vac (n = 89); 55 with IPV (see Supporting Information). The NPA against ancestral WT-B.1 (EPI_ISL_499083) and B.1.617.2 variant (EPI_ISL_6032417) in plasma was determined as previously described. 2 To compare the vaccines, IPV and the two viral variants were considered factors and incorporated in a mixed analysis of variance (ANOVA) analysis (taking sample as subject), using Student Newman Keuls as post-hoc (when ANOVA rejected Ho). NTAbs titers were used as response variables. The reciprocal of NTAb titers were transformed into base 2 LOG and the geometric mean titers (GMT) and antiLOG of GMT were calculated. Titers <1/10 were considered 1 and titers >1/640 were considered 1280. Soft R 3 was applied and in all cases, the significance level was 5%. Results showed that considering all the individuals evaluated altogether, a significantly lower NPA was observed against B.1.617.2 compared to ancestral WT-B.1 (GMT 5.8 vs. 3.7, respectively; p < 0.001). When

evaluating each group by condition, we detected a significant reduction in the NPA against B.1.617.2 in Group 1 and among individuals vaccinated with two doses of ChAdOx1-S, BBIBP-CorV, or Gam-COVID-Vac, with/without IPV (Figure 1). Group 1 presented a greater reduction of NPA against B.1.617.2 compared to WT-B.1, with a reduction of 2.6 in the GMT. Instead, in individuals vaccinated with BBIBP-CorV, ChAdOx1-S, or Gam-COVID-Vac with IPV, the decrease of GMT against B.1.617.2 compared to WT B.1 was 1.9, 1.5, and 1.4, respectively, while in those individuals without IPV, the reduction of GMT was higher: 2.3, 2.3, and 2.4, respectively (Table 1). Figure 1 Neutralizing activity of antibodies against B.1.617.2 versus wild type (WT) B.1 in the studied groups. Groups: (A) Unvaccinated and recovered from natural infection by SARS-CoV-2 wild type; (B) vaccinated with two doses of ChAdOx1-S; (C) vaccinated with two doses of BBIBP-CorV; (D) vaccinated with two doses of Gam-COVID-Vac. Violin Chart. Charts (B–D): Individuals without infection before vaccination are shown in gray and those with confirmed infection before vaccination are shown in orange. Graphics show geometric mean values and p values (Student Newman Keuls Test). Table 1 Comparison between different vaccines for neutralizing antibodies against SARS-CoV-2 WT B.1 and B.1.617.2

Vaccine	IPV	SARS-CoV-2 variant	Reciprocal of NTAb titers	LCI- 95%	UCI + 95%	GMT	SD	Group
BBIBP-CorV	No	B.1.617.2	4.32	3.57	5.22	2.11	0.14	A
ChAdOx1-S	No	B.1.617.2	5.43	4.49	6.56	2.44	0.14	AB
Gam-COVID-Vac	No	B.1.617.2	7.16	5.61	9.14	2.84	0.18	B
BBIBP-CorV	Yes	B.1.617.2	10.70	8.50	13.48	3.42	0.17	C
UR	Yes	B.1.617.2	13.93	11.06	17.55	3.80	0.17	C
BBIBP-CorV	No	WT B.1	20.68	17.10	25.01	4.37	0.14	D
ChAdOx1-S	No	WT B.1	27.47	22.72	33.23	4.78	0.14	DE
ChAdOx1-S	Yes	B.1.617.2	32.45	23.42	44.95	5.02	0.24	E
Gam-COVID-Vac	No	WT B.1	37.53	29.39	47.93	5.23	0.18	E
BBIBP-CorV	Yes	WT B.1	40.79	32.37	51.38	5.35	0.17	E
UR	Yes	WT B.1	85.63	67.97	107.87	6.42	0.17	F
ChAdOx1-S	Yes	WT B.1	94.35	68.10	130.73	6.56	0.24	F
Gam-COVID-Vac	Yes	B.1.617.2	121.10	98.77	148.47	6.92	0.15	F
Gam-COVID-Vac	Yes	WT B.1	308.69	251.78	378.46	8.27	0.15	G

Note: Results of the mixed ANOVA ($p < 0.001$) between the combination of vaccines, confirmed SARS-CoV-2 infection, and SARS-CoV-2 variant. GMTs within a common group are not significantly different ($p > 0.05$) according to ANOVA and Student Newman Keuls as post hoc. Abbreviations: ANOVA, analysis of variance; GMT, geometric mean titers; IPV, SARS-CoV-2 infection prior to vaccination; LCI − 95%, lower confidence interval of reciprocal of NTAb titers; SD, standard deviation; UCI + 95%, upper confidence interval of reciprocal of NTAb titers; UR, unvaccinated and recovered from infection by ancestral WT-B.1; WT, wild type. John Wiley & Sons, Ltd. The evaluation of vaccinated individuals showed that those immunized with Gam-COVID-Vac and

IPV achieved the highest titers of NTAb against B.1.617.2 (Figure 1D). When comparing the GMT against B.1.617.2 between the different groups of vaccinated individuals, there were no significant differences between those immunized with ChAdOx1-S and Gam-COVID-Vac or between ChAdOx1-S and BBIBP-CorV in subjects without IPV; however, we detected significant differences between groups immunized with Gam-COVID-Vac and BBIBP-CorV, respectively. In groups with IPV immunized with BBIBP-CorV or ChAdOx1-S, the GMT were 3.5 and 1.9 times lower than with Gam-COVID-Vac, respectively, yielding significant differences ($p < 0.001$; Table 1). Although significant differences were observed in NPA from recovered unvaccinated individuals compared to recovered and vaccinated with ChAdOx-1 or Gam-COVID-Vac ($p < 0.001$), there were no differences between NPA of unvaccinated recovered individuals versus those vaccinated with BBIBP-CorV ($p > 0.05$). The comparison between NPA against WT-B.1 and against B.1.617.2 evidenced that the last one decreased more than two GMT in all vaccinated individuals without IPV. The escape of B.1.617.2 variant from neutralization has been previously reported. [4,5,6] Nonetheless, we also show that among individuals with IPV, those immunized with BBIBP-CorV presented NTAbs titers against ancestral WT-B.1 significantly lower than unvaccinated individuals (GMT 5.35 and 6.42, respectively; $p < 0.001$). Moreover, NTAbs titers against B.1.617.2 were not significantly different between these groups (GMT 3.42 and 3.80, respectively; $p > 0.05$). Although the lack of cellular response and follow-up for clinical outcome and persistence of NTAb over time are limitations of this study, our findings strongly agree with those reported by Aijaz et al. [7] and Badano et al. [8] Since NTAbs titers against SARS-CoV-2 have demonstrated to be highly predictive of the host immune protection against infection, [9] our results, together with the previously mentioned studies, suggest that BBIBP-CorV would not be the most appropriate vaccine for individuals with IPV, since apparently, it does not contribute significantly to humoral immunity. Evaluation of the cellular response may explain the differences in NTAb response observed among individuals with IPV immunized with BBIBP-CorV. Our results showed that NTAb against SARS-CoV-2 elicited by natural infection and/or by immunization with two doses of Gam-COVID-Vac, ChAdOx-1 or BBIBP-CorV vaccines were able to neutralize the B.1.617.2 variant. However, there was a significant reduction in the NPA against SARS-CoV-2 B.1.617.2 variant.