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Omicron subvariants escape antibodies elicited by vaccination and BA.2.2 infection

The BA.1, BA.2, and BA.3 omicron subvariants of SARS-CoV-2 showed similar but substantial resistance to vaccine-induced and infection-induced serum neutralising activity.[1,2] The new BA.2.12.1, BA.2.13, BA.4, and BA.5 omicron subvariants containing Leu452 substitutions show more infectious potential than BA.2.[3] We examined neutralising activity against the BA.1, BA.2, BA.2.11, BA.2.12.1, BA.2.13, BA.4, and BA.5 omicron subvariants in serum from people who received BBIBP-CorV (Sinopharm) primary immunisation, people who received BBIBP-CorV or ZF2001 (Anhui Zhifei Longcom) boosters, and people with omicron breakthrough infections (appendix pp 4, 7).

25 individuals received two doses of BBIBP-CorV. Using an in-house pseudovirus neutralisation assay we found that two BBIBP-CorV doses induced detectable neutralising antibodies against spike protein mutation D614G in 21 (84%) individuals, but neutralising activity against omicron subvariants (BA.1, BA.2, BA.2.11, BA.2.12.1, BA.2.13, and BA.4/BA.5) was not or only minimally detectable (appendix pp 2–3, 8).

Geometric mean titres (GMTs) of neutralising antibodies against D614G in the 25 individuals who received a BBIBP-CorV booster were 3·1-times higher than in people who received two doses of BBIBP-CorV; the 30 people who received a ZF2001 booster had a 2·9-times higher GMT than individuals who received two doses of BBIBP-CorV (appendix pp 2–3, 8). Neutralising activity against omicron subvariants was observed in 24–48% of people who received a BBIBP-CorV booster and 30–53% of people who received a ZF2001 booster (appendix pp 2–3, 9). Moreover, serum samples with neutralising antibody titres higher than the limit of detection (limit of detection was 30) against the omicron subvariants had lower neutralising activity, with a 4·6–17·1-times lower GMT than the GMT against D614G (appendix pp 2–3). The BA.2.12.1 subvariant showed significantly more resistance than the BA.2 subvariant to a BBIBP-CorV booster (appendix p 9), and the BA.2.11, BA.2.12.1, and BA.2.13 subvariants showed significantly more resistance than the BA.2 subvariant to a ZF2001 booster (appendix p 9). The serum neutralising antibody titres against all tested pseudoviruses did not differ between people who received a BBIBP-CorV booster and those who received a ZF2001 booster (appendix pp 8–9).

18 people had BA.1 breakthrough infection and 15 people had BA.2.2 breakthrough infection (appendix pp 2–3, 7). People with BA.1 breakthrough infection had neutralising titres against omicron subvariants similar to neutralising titres against D614G except for BA.4/BA.5, which had a 2·8-times lower titre compared with D614G-mutated variants (appendix pp 2–3). Antibody titres against omicron subvariants BA.2, BA.2.11, BA.2.12.1, BA.2.13, and BA.4/BA.5 were similar to antibody titres against BA.1 (appendix pp 2–3). Additionally, neutralising antibodies against omicron subvariants above the limit of detection accounted for 88–100% of infections. By contrast, BA.2.2 breakthrough infections had small increases in GMTs against BA.1 compared with BA.1 breakthrough infections (appendix p 10), and neutralising titres against all omicron subvariants, except BA.2, were significantly decreased (3·5–7·4 times) compared with the titres against D614G (appendix pp 2–3). BA.2.2 breakthrough infection resulted in 73–87% of individuals having neutralising antibodies against omicron subvariants higher than the limit of detection (appendix pp 2–3), but neutralising antibody titres against BA.2 were significantly higher than other omicron subvariants (appendix pp 2–3). People with BA.1 breakthrough infections had significantly higher neutralising antibody titres against the BA.1 and BA.2.13 subvariants than people with BA.2.2 breakthrough infections (appendix p 10). Of note, compared with the people with a BA.1 breakthrough infection, people with BA.2.2 breakthrough infections included a substantially higher number of individuals who were triple vaccinated (appendix p 7).

Completion of the primary BBIBP-CorV vaccination schedule induces neutralising antibodies in most individuals against SARS-CoV-2 variants with a D614G mutation, which is consistent with previous studies.[4–6] However, the spike protein mutation enables the escape of omicron subvariants from neutralisation, which can be partly restored by a booster vaccination. Breakthrough omicron infections enhance sera neutralising potential specifically against the omicron subvariants, which is consistent with two recent studies.[7,8] Together, our results indicate that the new SARS-CoV-2 subvariants (eg, BA.2.12.1 and BA.4 and BA.5) could cause a new wave of infections.

See Online for appendix

We declare no competing interests. LY, K-LZ, X-LJ, X-JW, and B-DZ contributed equally.

*Lin Yao, Ka-Li Zhu, Xiao-Lin Jiang, Xue-Jun Wang, Bing-Dong Zhan, Hui-Xia Gao, Xing-Yi Geng, Li-Jun Duan, Er-Hei Dai, *Mai-Juan Ma*
mjma@163.com

State Key Laboratory of Pathogen and Biosecurity, Beijing Institute of Microbiology and Epidemiology, Beijing, China (LY, K-LZ, X-JW, L-JD, M-JM); Department of Epidemiology and Biostatistics, School of Public Health, Anhui Medical University, Hefei, China (LY, K-LZ, M-JM); Shandong Provincial Key Laboratory of Infectious Disease Control and Prevention, Shandong Provincial Center for Disease Control and Prevention, Jinan, China (X-LJ); Department of Laboratory Medicine, Quzhou Center for Disease Control and Prevention, Quzhou, China (B-DZ); Department of Laboratory Medicine, The Fifth Hospital of Shijiazhuang, Hebei Medical University, Shijiazhuang, China (H-XG, E-HD); Department of

Infectious Disease Control and Prevention, Jinan Center for Disease Control and Prevention, Jinan, China (X-YG)

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