

Follow-up and comparative assessment of SARS-CoV-2 IgA, IgG, neutralizing, and total antibody responses after BNT162b2 or mRNA-1273 heterologous booster vaccination

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Abstract

Background: Priming with ChAdOx1 followed by heterologous boosting have been considered in several countries. Nevertheless, analyses that provide a comparison of the immunogenicity of heterologous booster in comparison to homologous primary vaccination regimens and natural infection are lacking. In this study, we aimed to conduct a comparative assessment of the immunogenicity between heterologous prime-boost vaccination using BNT162b2 or mRNA-1273 and homologous primary vaccination regimens. Methods: We matched vaccinated naïve individuals (VN; n=673) who had received partial vaccination (n=64), primary vaccination (n=590), or primary series plus one mRNA vaccine heterologous booster (n=19) with individuals with a documented primary SARS-CoV-2 infection and no vaccination record (natural infection; NI cohort; n=206). We measured the levels of neutralizing total antibodies (NTAbs), total antibodies (TAb), anti-S-RBD IgG, and anti-S1 IgA titers. Results: Homologous primary vaccination with ChAdOx1 not only showed less potent NTAbs, TAb, anti-S-RBD IgG, and anti-S1 IgA immune responses compared to primary-BNT162b2 or mRNA-1273 vaccination regimens ($P < 0.05$), but also showed ~3 fold less anti-S1 IgA response compared to infection-induced immunity ($P < 0.001$). Nevertheless, heterologous booster dose resulted in a significant boost of at least ~12 folds in the immune response. Furthermore, correlation analyses revealed that both, anti-S-RBD IgG and anti-S1 IgA significantly contributed to virus neutralization among NI individuals, particularly in symptomatic and pauci-symptomatic individuals, whereas, among VN individuals, anti-S-RBD IgG was the main contributor to virus neutralization ($r > 0.90$, $P < 0.001$). Conclusion: The results emphasize the potential benefit of using heterologous mRNA boosters to increase antibody levels and neutralizing capacity.

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