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Spike antibody seroconversion and breadth following SARS-CoV-2 vaccination in Australian people with multiple sclerosis

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Background: COVID-19 vaccination induces protective Spike antibodies. Some responses are attenuated in people with multiple sclerosis (MS) on high efficacy disease-modifying therapies (DMT).Whether antibodies afford immunity against emerging SARS-CoV-2 Variants of Concern (VoC) such as Delta and Omicron is unknown.
Aims: To assess the longevity and breadth of Spike antibody in MS patients after COVID-19 vaccination.
Objective: To determine seroconversion and antibody binding toVoC Spike.
Methods: Spike antibodies to Clade A SARS-CoV-2 were assessed in 535 MS sera at baseline (n=292), 1 (n=141) and 6 month (n=67) post-second dose, and 1 month post-third dose (n=35), and 489 health worker controls. When known, COVID-19 vaccines were BNT162b2 (n= 489 controls, n=108 MS patients) and ChAdOx1-S (n=37).Spike antibody binding to VoC Delta and Omicron BA1 was assessed in 68 sera 1 month post-second dose. Demographic and DMT information was available in 269 patients.
Results: 123/141 sera at 1 month post-second dose, 66/67 at 6 months post-second dose, and 26/35 at 1 month post-third dose were positive for Spike antibodies.Patients who did not seroconvert at 1 and 6 month post-second and 1 month post-third dose (n=28) were treated with ocrelizumab (n=22), cladribine (n=1), fingolimod (n=4), and siponimod (n=1). At 1 month post-second dose, the median and IQR Spike antibody levels were 67,224± 101,251 in the seroconverted MS group compared to 145,510± 99,669 in controls (n=489). When patient sera were assessed for binding to Clade A Spike, and VoC Delta and Omicron BA1 Spikes, most sera were able to bind the three different Spike antigens (n=61). However,Spike antibody immunoreactivity was decreased by 70% against Delta Spike and 90% for Omicron BA1 Spike compared to the original clade A Spike.As observed for Clade A Spike antibody, DMTs, such as ocrelizumab, fingolimod, and ofatumumab, decreased the antibody binding to Delta and Omicron Spike. Still, the pattern of antibody recognition was similar between the three Spikes and all DMTs analysed, i.e. alemtuzumab, natalizumab, teriflunomide, and interferons. Our data suggest that,irrespectively of DMTs, antibodies generated after vaccination did not bind Spike from recent VoCs to the same extent as the original Spike used in COVID-19 vaccines.
Conclusions: Some DMTs reduce Spike antibody titres or prevent seroconversion. The sequence of Spike used in the first generation of vaccines may need to be updated for emerging VoC.
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