Inflammatory bowel disease biologic blunts immune response to COVID-19

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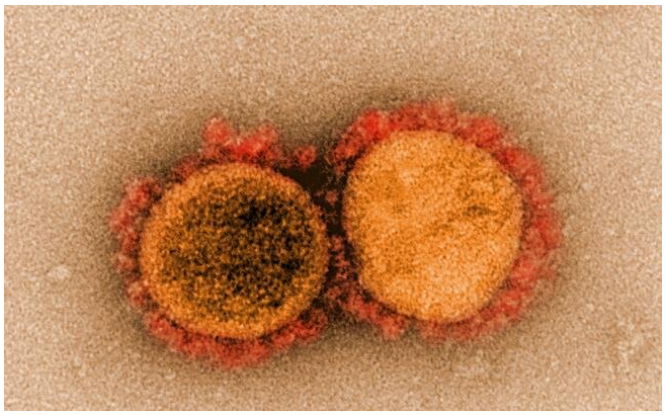

Transmission electron micrograph of SARS-CoV-2 virus particles, isolated from a patient. Image captured and color-enhanced at the NIAID Integrated Research Facility (IRF) in Fort Detrick, Maryland. Credit: NIAID

Careful monitoring of patients treated with infliximab needed after COVID jab

Infliximab, a powerful biologic that is used to treat inflammatory bowel disease (IBD), blunts the body's immune response to COVID-19 infection, indicates research published online in the journal *Gut*.

This impaired response may boost susceptibility to recurrent COVID-19 and help drive the evolution of new variants of SARS-CoV-2, the virus responsible for the infection, warn the researchers.

Careful monitoring of IBD patients treated with infliximab will be needed after vaccination against COVD-19 to ensure they mount a strong enough antibody response to ward off the infection, they advise.

Infliximab belongs to a class of medicines called anti-tumour necrosis factor (anti-TNF) drugs. These drugs suppress the production of an inflammatory protein involved in the development of several conditions, including ulcerative colitis and Crohn's disease which are types of inflammatory bowel disease.

Around 2 million people worldwide are treated with anti-TNF drugs, which are known to impair protective immunity following vaccination against pneumonia, flu, and viral hepatitis, as well as increasing the risk of serious infection, particularly respiratory infections.

Because of these risks, patients taking these drugs have been advised to shield during the coronavirus pandemic and/or take extra precautions to minimise their risk of catching COVID-19.

With these issues in mind, the researchers wanted to find out if anti-TNF drugs might blunt the body's immune response to SARS-CoV-2 as well. They therefore compared the antibody responses to SARS-CoV-2 in IBD patients treated with infliximab or another biologic called vedolizumab.

Vedolizumab is a gut monoclonal antibody that has a dosing schedule similar to that of infliximab. But it isn't associated with increased susceptibility to systemic infection or blunted immune responses to vaccination.

In all, 6935 IBD patients (average age 39) were recruited from 92 UK hospitals between September and December 2020 for the CLARITY IBD study: around two thirds (4685) of them were being treated with infliximab and around a third (2250) with vedolizumab.

Nearly 40% (2589 out of 6935) had been swab (PRC) tested for SARS-CoV-2. And rates of symptomatic and confirmed SARS CoV-2 infection were similar in both treatment groups.

Some 389 (8%) of the infliximab group and 201(9%) of the vedolizumab group had symptoms

indicative of COVID-19 infection; 89 out of 1712 of those taking infliximab tested positive for the virus (just over 5%) as did 38 out of 877 (just over 4%) of those taking vedolizumab.

But fewer patients treated with infliximab had detectable antibodies to the virus in their blood than those treated with vedolizumab: 3.4% (161/4685) vs 6% (134/2250).

And only around half (48%; 39/81) of the patients treated with infliximab whose COVID-19 infection was confirmed by a swab test subsequently developed antibodies compared to 83% (30/36) of those treated with vedolizumab.

And the addition of other commonly used drugs to dampen down the inflammatory response, such as thiopurine or methotrexate, further blunted the antibody response to SARS-CoV-2 in patients treated with infliximab, only a third of whom had detectable antibodies to SARS-CoV-2.

An increase in antibodies to SARS-CoV-2 was observed 4 weeks after a positive swab test in patients taking vedolizumab, but not in those treated with infliximab.

"Similar rates of symptomatic and proven SARS-CoV-2 infection and hospitalisations between infliximab-treated and vedolizumab-treated patients suggest that our findings cannot be explained by differences in acquisition or severity of infection alone. Rather, infliximab seems to be directly influencing the serological response to infection," explain the researchers.

"Infliximab may directly impede the immune mechanisms responsible for generating antibody responses," they suggest.

This is an observational study, and so can't establish cause. And the researchers acknowledge certain limitations to their study, including that weakened immune responses in patients treated with infliximab don't automatically translate into a heightened risk of infection.

Protective immunity after vaccination involves more than just antibodies. And the only anti-TNF drug studied was infliximab.

Nevertheless, they suggest that a weakened antibody response has potentially far reaching implications.

It may increase susceptibility to recurrent COVID-19 in patients treated with infliximab, which might then lead to chronic colonisation of the virus in the nose and throat. This "may act as a reservoir to drive persistent transmission and the evolution of new SARS-CoV-2 variants," they warn.

And they conclude: "Serological testing and virus surveillance should be considered to detect suboptimal vaccine responses, persistent infection, and viral evolution to inform public health policy.

"If attenuated serological responses following vaccination are also observed, then modified immunisation strategies will need to be designed for millions of patients worldwide."

More information: Anti-SARS-CoV-2 antibody responses are attenuated in patients with IBD treated with infliximab, *Gut* (2021). DOI: 10.1136/gutjnl-2021-324388

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