EVIDENCE-BASED GI
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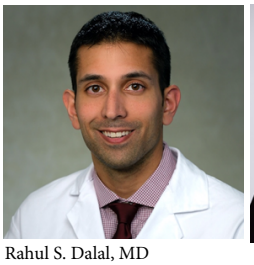
IBD

Infliximab Therapy Is Associated with Reduced Antibody Responses Against SARS-CoV-2



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This article reviews Kennedy NA, Goodhand JR, Bewshea C, et al. Anti-SARS-CoV-2 antibody response are attenuated in patients with IBD treated with infliximab. Gut 2021; 70: 865-75. PMID: 33753421
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STRUCTURED ABSTRACT

Question: Are anti-SARS-CoV antibody responses attenuated among IBD patients treated with infliximab, an anti-tumor necrosis factor (anti-TNF) agent which may suppress immune responses compared to IBD patients treated with vedolizumab, a gut-specific monoclonal antibody that is not associated with increased risk of systemic infection or attenuated serological response to vaccination?

Design: Prospective observational cohort study.

Setting: Infusion units from 92 National Health Service hospitals across the United Kingdom.

Patients: A total of 7,226 patients with inflammatory bowel disease (IBD) were enrolled between September 2020 and December 2020. Median age was 39 years, 88.4% of patients were White, 46.4% were female, and 56.9% had Crohn's disease. Patients were required to be treated with infliximab (67.6%) or vedolizumab (32.4%) for 6 or more weeks and at least 1 dose in the past 16 weeks. Those who participated in prior SARS-CoV-2 vaccine trials were excluded.

Exposure: The main exposures were infliximab vs vedolizumab therapy among patients with IBD.

Outcome: Proportion of IBD patients with positive anti-SARS-CoV antibody test.

Data Analysis: Rates of antibody seroconversion among patients overall and among those with confirmed COVID-19 infection based on a positive PCR test to SARS-CoV-2 were compared between biologic group using Fisher's exact and Mann-Whitney U tests. Multivariable logistic regression was used to identify factors independently associated with seropositivity for SARS-CoV-2.

Funding: The study was funded by F. Hoffmann-La Roche, Hull University Teaching Hospital NHS Trust, Biogen GmbH, Celltrion Healthcare, Galapagos NV, Royal Devon, and the Exeter NHS Foundation Trust.

Results: Seroprevalence for anti-SARS-CoV-2 antibody was lower among infliximab-treated patients compared to vedolizumab-treated patients. Among patients with confirmed COVID-19 infection based on a positive PCR test, there were lower rates of antibody seroconversion among infliximab-treated patients compared to vedolizumab-treated patients **(Table 1)**. On multivariable analysis, infliximab and immunomodulator use were independently associated with lower seropositivity.

Exposures overall	**SARS-CoV-2 Seropositivity**			***P*-value**
Biologic				<0.01
Infliximab	3.4%			
Vedolizumab	6.0%			
Biologic +/- immunomodulator				<0.01
Infliximab monotherapy	4.1%			
Infliximab + immunomodulator	3.0%			
Vedolizumab monotherapy	6.3%			
Vedolizumab + immunomodulator	4.5%			
Exposures in patients with confirmed SARS-CoV-2 infection	**SARS-CoV-2 Seropositivity**	***P*-value**	**Antibody reactivity (COI)**	***P*-value**
Biologic		<0.01		<0.01
Infliximab	48%		14.5	
Vedolizumab	83%		47.2	

Table 1. Summary of findings.
COI, cut off index. The COI is a quantitative measure of magnitude of antibody response.

COMMENTARY

Why Is This Important?

Unlike vedolizumab, anti-TNF agents such as infliximab are known to blunt antibody-mediated immune responses. Patients with IBD appear to be at similar risk for infection and illness severity for COVID-19 regardless of type of biologic therapy.[1,2] However, relative serologic responses and protection after exposure to SARS-CoV-2 are unknown.

The results of the study suggest that patients treated with infliximab are less likely to mount an anti-SARS-CoV-2 antibody response and also have a lower magnitude of antibody reactivity when compared vedolizumab-treated patients with IBD. This raises concern that patients receiving anti-TNF agents may have less protection against COVID-19 after exposure or vaccination. A recent study supports this suspicion, as patients treated with infliximab had lower anti-SARS-CoV-2 antibody concentrations after a single vaccine dose compared to patients treated with vedolizumab.[3] After 2 vaccine doses, seroconversion was observed for the majority of patients. However, another prospective study observed a lower magnitude of antibody response after 2 mRNA vaccine doses among anti-TNF-treated patients.[4] In a recent analysis of 528 patients with IBD, 99% achieved detectable antibodies 2 weeks after the second dose of an mRNA vaccine regardless of medication regimen.[5] However, patients receiving combination therapy with an anti-TNF and immunomodulator had the lowest level of detectable antibodies. In combination, these findings justify a proactive and perhaps more intensive approach towards vaccination for the anti-TNF-treated population. Gastroenterologists should consider these data when counseling immunosuppressed patients whose vaccination hesitancy stems from the assumption that prior COVID-19 infection confers immunity.

Key Study Findings

The authors found that the seroprevalence of anti-SARS-CoV-2 antibodies was lower among IBD patients treated with infliximab compared to vedolizumab. Among patients with COVID-19 infection confirmed by PCR testing, there were lower rates of antibody responses and a lower magnitude of antibody reactivity among those treated with infliximab compared to vedolizumab. On multivariable analysis, infliximab and immunomodulator use were independently associated with lower anti-SARS-CoV-2 antibody seropositivity.

Caution

While the study identified reduced antibody responses among infliximab-treated patients, other forms of immune responses, such as T-cell responses, were not investigated. Additionally, other anti-TNF agents such as adalimumab, golimumab, and certolizumab were not included in this study.

Therefore, it is unknown if the findings will translate to a higher risk of COVID-19 infection for patients treated with anti-TNF agents in general.

My Practice

I encourage all of my patients to receive one of the FDA-approved COVID-19 vaccines, which are safe and effective. I advise my IBD patients on immunomodulators, corticosteroids, and biologics to receive a booster dose of the vaccine, including those on less systemically immunosuppressive agents such as vedolizumab. Acknowledging the possibility of breakthrough infections, I continue to emphasize mask-wearing, frequent hand washing, avoidance of large indoor gatherings, and staying home when infectious symptoms arise.

For Future Research

A growing body of evidence suggests that anti-SARS-CoV-2 antibody responses are suppressed with anti-TNF agents. What remains unclear is if infectious risks are also increased, and if multiple booster doses may be beneficial for these individuals. Future research should attempt to compare the long-term rate of SARS-CoV-2 breakthrough infections between biologic classes and determine the clinical applications of post-vaccination serological testing.

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