Is Vedolizumab Truly Gut Selective? It May Not Affect the Immunogenicity of Vaccines in Patients With Inflammatory Bowel Disease

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Optimal medical therapy for inflammatory bowel disease (IBD) often includes the use of a single or a combination of immunosuppressive medications including immunomodulators and monoclonal antibodies, such as antitumor necrosis factor alpha (TNF-α) and anti-integrin agents.[1] Unfortunately the use of such therapies is associated with a further increased risk of serious and opportunistic infections, including vaccine preventable diseases (VPDs).[2,3] The risk of some of these infections can be mitigated by routine immunization including influenza, pneumococcal pneumonia, and herpes zoster. Thus, gastroenterologists should assume or share the responsibility with primary care providers to ensure their patients with IBD are up to date with appropriate vaccines.[4] Regretfully, anti-TNF therapy may blunt the immune response to certain vaccines and reduce their efficacy. Prior studies have found patients on anti-TNF are more likely to have a blunted immune response to the influenza vaccine and may benefit from an altered immunization schedule.[5,6] There are limited data on the impact of vedolizumab or ustekinumab on the immune response to vaccines.

Vedolizumab, a gut-selective monoclonal antibody that targets $\alpha_4\beta_7$ integrin, is an effective treatment for moderate to severe IBD. Presumably due to its ability to selectively target and block lymphocyte trafficking to the intestinal tract, prior studies have shown a favorable safety profile without an increased risk of respiratory tract or serious infections when compared to placebo.[7,8] Its effect on vaccine immunogenicity is not well-established. The study by Harrington et al aimed to examine the effect of vedolizumab on vaccine immune response. They conducted a single-center, prospective controlled trial investigating the immunogenicity and safety of the influenza, pneumococcal, and hepatitis B vaccines in patients with IBD treated with vedolizumab compared to other immunosuppressive regimens.[9] Patients were enrolled over a time period spanning 2 influenza seasons and subdivided into 4 groups based upon their IBD treatment regimen (vedolizumab monotherapy, vedolizumab combination therapy, anti-TNF combination therapy, or no immunosuppressive therapy). They provided 160 vaccines over the study period with 48 vaccines administered to 25 patients on either vedolizumab mono- or combination therapy. Overall, they found that vedolizumab therapy did not diminish the immunogenicity of the vaccines compared to the other treatment regimens. For the influenza vaccine, no groups met criteria for adequate response but this was attributed to high baseline titers across all study participants. For the pneumococcal vaccines, all groups had an immunogenic response with no statistically significant differences between groups, and patients on vedolizumab had a noninferior response to hepatitis B vaccine compared to the control group. Notably, there were no serious adverse events or significant changes in disease activity found during the study period.

The results of this study suggest the use of vedolizumab in patients with IBD does not dampen the immune response to these vaccines compared to anti-TNF treatment regimens with comparable titer response rates to the nonimmunosuppressed control group. Furthermore, vaccinations are well tolerated without an appreciable effect on disease activity and should continue to be recommended in accordance to current guidelines.[4] The prospective evaluation of vedolizumab on the immune response to influenza, pneumococcal, and hepatitis B vaccines in patients with IBD are major strengths of the study. Doing so with the inclusion of an IBD control group rather than healthy controls significantly expands the study's external validity. The limitations of the study were readily recognized by the authors, namely the lack of observed seroconversion to the influenza vaccine and small sample size across all groups.

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Due to high baseline influenza antibody titers, seroconversion, defined as a 4-fold increase in antibody titers, was unable to be attained. As higher antibody concentrations induced by vaccinations have been associated with better protection against infection, reporting seropositivity based upon a defined antibody threshold would likely have been more informative rather than evaluating for seroconversion.[10] As a result, the diminished response to the influenza vaccine by anti-TNF therapy observed from prior studies was not appreciated, thus limiting the study's ability to measure a difference between anti-TNF and anti-integrin therapy. Furthermore, the small sample size necessitated combining the groups on vedolizumab mono- and combination therapy for analysis. This limited the power of the study to detect a potential blunted response of combination immunomodulatory therapy. Despite these limitations, these are clinically impactful findings to an important question posed by Harrington et al. Since, infections remain a common complication of immunosuppressive regimens in patients with IBD and it is imperative to mitigate the risk of VPD.

To date, this is the largest prospective analysis evaluating the impact of vedolizumab on the immune response to vaccines. The results are consistent with the findings by Wyant et al who concluded vedolizumab does not affect the immune response to the parenterally administered hepatitis B vaccine.[11] It is important to note Wyant et al evaluated the immunogenicity of healthy individuals without IBD following a single vedolizumab infusion. In contrast, this study required all participants to be on stable maintenance dosing for at least 3 months prior to vaccine administration, making their findings more generalizable. Two recently published studies evaluating the immunogenicity of influenza and pneumococcal vaccines further support these findings. A large study evaluating the immunogenicity of PCV13 in patients with IBD found that patients on vedolizumab had similar rates of seroprotection compared to those on 5-aminosalicylates and/or topical corticosteroids. Their outcomes are limited as only 26 patients were on vedolizumab, making it difficult to extrapolate these findings.[12] A study evaluating the immunogenicity of the high-dose influenza vaccine in patients with IBD on anti-TNF therapy also included 19 IBD patients on vedolizumab as a comparator group.[6] Those on vedolizumab had equivalent antibody concentrations to healthy controls after receiving the standard dose influenza vaccine as well as the high-dose anti-TNF group, providing further evidence that anti-integrin therapy may not impact the immunogenicity of the influenza vaccine. The results of all these studies are limited by the small sample size and larger studies are needed to determine if vedolizumab has an impact on the immune response to certain vaccines.

Understanding the safety and efficacy of vaccines in patients with IBD remains an important area of research. There is mounting evidence that vaccines are well tolerated without an increased risk of exacerbating disease activity in IBD. This is particularly significant now amid the COVID-19 pandemic and a future COVID-19 vaccine. It will be paramount to determine if patients with IBD on certain immunosuppressive regimens are at risk for a blunted COVID-19 vaccine response and may need an alternative immunization schedule. Furthermore, as advances in IBD therapy expand the treatment armamentarium, it will be necessary to continue to investigate the impact of novel new agents, such as Janus Kinase inhibitors and others, on the immunogenicity of vaccines. Additionally, as the management of IBD becomes more complex, it may not be long before combination biologic therapy becomes commonplace. The use of multiple agents may further impact the immune response to vaccines and will need to be evaluated to decrease the risk of VPD. Collaborative research efforts will be needed to allow for large, multicenter prospective trials to further the research conducted by Harrington et al.

DATA AVAILABILITY

Data sharing is not applicable to this article as no new data were created or analyzed.

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