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Investigating the Impact: IBD Therapies & Contracting COVID-19

Dr. Nandi:
Welcome to *GI insights* on ReachMD. I'm Dr. Neil Nandi. Today, we will be answering some of the most common questions regarding COVID-19 in our IBD patients. Indeed, the modern world has been forever changed with the effects of the coronavirus pandemic. Johns Hopkins University data report that as of March 19th, 2021, there have been nearly 30 million cases of coronavirus in the USA alone, with over 540,000 reported deaths. The Secure IBD registry aggregates clinician-documented cases of IBD patients with COVID-19 worldwide. In the United States as of March 19th, 2021, the registry reports 2,087 cases of IBD patients in the USA with COVID-19 with 12 reported deaths. On the whole, the numbers are small, but of course every life lost is tragic. Fortunately, these small numbers are encouraging, and we know far more than we did just one year ago.

Today we'll specifically be reviewing the effect of IBD therapies on contracting coronavirus. Also related, but distinctly different, the management of IBD treatments in a patient who's developed COVID-19 illness.

Joining me to defeat myth and misconception with truth is one of our truest IBD authorities, Dr. David Rubin. Dr. David Rubin is a Professor of Medicine at the University of Chicago Pritzker School of Medicine. He is the Section Chief of the Division of Gastroenterology, Hepatology and Nutrition, and Co-Director of the Digestive Diseases Center. Notably, he is a recipient of the 2020 Sherman Prize for his unwavering commitment to IBD clinical care, research excellence, and patient advocacy. Welcome to *GI Insights*, Dr. Rubin.

Dr. Rubin:
Hey, Dr. Nandi, thank you so much for having me. I'm excited to have this conversation.

Dr. Nandi:
We're very pleased to have you. Now, no doubt we've come a long way and we understand some of the effects of our IBD therapies on COVID-19. Can you give our clinicians a brief synopsis of what are the risks of biologics, or thiopurines, or mesalamine on developing COVID or severity in COVID?

Dr. Rubin:
This is an important topic because the patients who have inflammatory bowel disease have a recognized defect or dysregulation of their immune system at baseline. And the therapies we use to treat inflammatory bowel disease, for the most part, are immune based, meaning that they are designed to target the immune system in order to control that overactive immunity. So, when we talk about an infectious disease like COVID-19, we have to be nervous about our patients with these conditions because they have problems with their immune system and they're on therapies that reduce their immune overactivity.

So, it's a natural question to want to know, are people with Crohn's disease and ulcerative colitis at a higher risk for contracting coronavirus infections? And are they therefore at a higher risk for COVID? And if they are, do they have worse or better outcomes when they get COVID? The short answer is that we have, across multiple countries and an international registry, demonstrated that patients with inflammatory bowel disease in general are not at increased risk for contracting the coronavirus that we call SARS-CoV2, nor are they at increased risk for getting COVID-19 if they get infected. And for the most part, with a couple exceptions we'll talk about, they are not at risk for worse outcomes from COVID-19. So, the main message to the patients with inflammatory bowel disease, which we hoped for in the beginning of the pandemic and has been further confirmed with the research we have so far, is that people with IBD are not at increased risk. That doesn't mean they're a decreased risk necessarily but that they should be reassured, and they should stay on their stable therapies.

Dr. Nandi:
This is really helpful for us to put out there into the ether because we still hear patients who are living in a tight bubble, right? They think that their biologic or small molecule therapy is putting them at higher risk.

So what happens, though, if a patient contracts coronavirus and actually develops symptoms of COVID-19, tests positive, and we get that phone call at the end of the day? What should we be advising them? And how does the biologic, or small molecule therapy, or steroid affect how we should advise them what to do?

Dr. Rubin:
Well, there's a couple of different categories to think about. The first one is if somebody actually has symptoms of COVID-19. Remember, that's predominantly respiratory symptoms, shortness of breath, cough, congestion loss of taste or smell, but can also involve digestive disease symptoms. And that can be diarrhea or abdominal pain, which obviously, in an IBD patient, would be of concern and confusing to us. If they test positive for the SARS-CoV2, and they have those symptoms, and we diagnose them with COVID-19, the question then becomes, what do you do with therapy they're already on? Do you stop it? Do you continue it? Or do you change it to something else?

The International Organization for the Study of IBD developed a consensus statement about this, and then evidence supports what they recommended early on. So, when we talked about this in the early days, we said, “Well, if somebody becomes infected and has COVID-19, we would just, from a rational point of view, say, ‘Stop the immune suppressive therapy, at least for the two-week period of time that they're sick.’” And when they recover from the COVID-19, they could resume the therapy. Now, that would include our thiopurine, methotrexate, biologics, small molecule like tofacitinib, with the general strategy of, “Why would you give ongoing immune therapy in the face of a disease caused by an infectious organism?” What we have subsequently learned and the practical reality is that the half-life of all these drugs is such that even if you're holding it for a little bit, the drug is still on board. So, what are we really doing? Are we just treating ourselves or does it make practical sense to hold the therapy during that short interval?

And the answer is there have now been many examples of patients who had COVID that didn't stop their medicine. And those who had COVID, and we held their medicine as their doctors, and their outcomes look the same. Now, that doesn't mean we should just leave people on immunosuppressive therapy when they get sick, but it does reassure us that at least the therapies we use for IBD may not be harming our patients even when they develop COVID-19.

Now, to be more granular, there are a couple exceptions. One is that we now know in multiple studies that people who are on steroids at doses higher than 20 milligrams a day at the time they get infected are at higher risk for having worse COVID outcomes. Now, this is contrary to the randomized controlled study of steroids at the time, people had COVID and were having respiratory problems and were in the ICU. That study, which was called RECOVERY, run out of the UK, showed that later in the illness, when you have respiratory problems, steroids may actually be helpful. But in this specific situation, for many of our IBD patients who are on steroids when they get sick, we've learned that that sets them up for worse outcomes. And an immediate strategy to get them down or off steroids in that setting is absolutely important.

Otherwise, our therapies, we have come to believe, are not going to hurt our patients. And although it's reasonable to pause them, we don't need to be overly alarmed by that at all.

There may even be a benefit to these therapies in certain scenarios. For example, the nonselective Janus kinase inhibitor, tofacitinib, and other JAK inhibitors, are being studied as treatments for the inflammatory phase of COVID, as are anti-TNF therapies, specifically adalimumab. So, the treatments we have patients on may actually end up benefiting those patients later. In at least one analysis from the International Registry called SECURE IBD, being on an anti-TNF was associated with lower risk of some bad outcomes from COVID-19.

The other issue then is what if you have somebody who is asymptomatic but tests positive? And remember, that's a key feature of the SARS-CoV2 that led to this being a pandemic is that people were asymptomatic but carriers and transmitting the virus. In that setting, we have said that you should pause your immune therapies for at least 10 days and wait to see if the patient becomes symptomatic. And then you can resume therapy if nothing happens. That's a precaution. Now there's probably been a lot of people who were asymptomatic, never developed the disease or developed very mild symptoms that they didn't even realize, and stayed on their therapy, and therefore, we probably don't have to worry about them as much.

So that's the main strategy to these different scenarios. And I think the important thing we've done is reminding our patients to continue doing the other precautions, which is, of course, to wear a mask and to social distance when they can or physically distance in other ways and, of course, hand hygiene.

Dr. Nandi:

For those just tuning in, you're listening to GI Insights on ReachMD. I'm Dr. Neil Nandi, and today I'm speaking with Dr. David Rubin about IBD medications and their management in COVID-19.

Now, Dr Rubin, there's currently a handful of research out there about COVID-19 and patients with IBD. Could you expand on some of the research you've been seeing and what it means for our patients?

Dr. Rubin:
There's two points I want to make. One of them is that the SECURE IBD registry, which is this online open access registry that is composed of people who voluntarily enter their patients with confirmed IBD and who know the outcome of their illness. And one of the things that came out in a subsequent analysis and is in press in *Gut* right now by the people leading this work, is that patients who are on file on thiopurines or on combo therapy with a thiopurine and an anti-TNF had worse outcomes from COVID. Now, this was not seen in a single country study in Italy where they described the outcome of 79 patients with COVID and where they admittedly knew a little bit more about the disease in that study than was allowed in the registry study of SECURE IBD. But it raises our eyebrows to wonder whether thiopurines might be associated with worse outcomes. And previously we hypothesized that because thiopurines reduce white blood cell count, it might be associated with worse COVID outcomes. Remember that some people with severe COVID had drops in their lymphocyte counts that were predictive or associated with those worse outcomes.

It lends itself to the question of if you have a patient on combo therapy, would you stop the thiopurine and leave them on the biologic alone? Either now, because we're still in the pandemic, or if your patient got ill and had COVID. And the general recommendation is if they get COVID, we hold our therapies, even though we didn't know if that was going to help. But we do. So that sort of answers itself. I personally have not withdrawn combo therapy in my patients. I have just advised them to continue doing the precautions we recommend for everybody. And I think that we need to understand further whether this was just the sickest patients who might have had the worst IBD who were on combo therapy to begin with, and therefore, there was a confounder there that's not adjusted or something else.

The other thing that came out of this and has appeared in different ways was that patients on mesalamine might have had worse outcomes. Now we have yet to identify a rational biologic explanation for why that would be. But one possibility that's been raised is that people on mesalamine may have also had active IBD. And because their disease was less well controlled. And given that the SECURE IBD registry is an international registry where 5-ASA use in Crohn's as well as colitis is still the number one therapy, it may have been an over accessed and measured drug exposure.

So that isn't entirely clear either. And I don't think any of us would say, "You should stop 5-ASAs during the pandemic" in a patient who is in stable remission. So that doesn't quite make sense, despite many people trying to understand it or to know better what might be going on there.

The second point I wanted to make is related to a study in Germany where they actually looked at people not just with IBD but with other immune conditions as well who were on anti-cytokine therapies. That means anti-TNF, anti-IL23, or JAK inhibitor therapies. And they compared them to those who had the same diseases but weren't on those therapies and to healthcare workers. And they adjusted for exposures at work, whether you were working in an environment where you might get exposed to COVID. And they actually found that the people with the immune conditions on anti-cytokine therapies were less likely to have antibodies against the SARS-CoV2. In other words, they were less likely to have developed immunity or possibly less likely to have gotten sick or infected. And so, it raised this interesting hypothesis that people on these drugs may actually be protected. The counterargument is just that, as you mentioned, people may be taking more precautions because they're afraid, but they tried to adjust that in that study. It's a fascinating study from Germany.

Dr. Nandi:
In closing, I want to ask one last thing, which is let's say we have a patient who has had COVID, and is recovered from it, any advice on the timing of when they should receive a vaccine?

Dr. Rubin:
It's been recommended that if you have test positive COVID or strongly suspected to have had COVID that you get vaccinated and that you get vaccinated 90 days or more after you've been infected. It's also important to recognize that although having an infection may induce immunity, it doesn't seem to have the same durability as the immunity that would be obtained by being vaccinated. So somebody may say, well, I had COVID so I don't need to be vaccinated. That's incorrect. You should still get vaccinated. Just like we say, by the way, of someone who's had shingles, they still should be getting vaccinated in the appropriate populations and at the right time against shingles. It's the same concept here. You may have had COVID, but that doesn't necessarily mean you're protected from it the way a vaccine will do it for you.

Dr. Nandi:
Yeah, you know, I remember there was a time a year ago where we were conscious of the fact that there may not be a vaccine, that we would possibly not be successful in developing a vaccine at all. And it's a true miracle that now we're sitting here with three different vaccines. And again, I think the take-home message is today for our IBD patients and for clinicians who take care of them are your patients should receive the vaccine that is available to them, that it is safe that it is not going to cause them harm or flare and that there is hope for a brighter future with them aboard.

Dr. Rubin, thank you so much for your time, your wisdom, your insights. As always, you're absolutely spot-on in the education that you provide us. We're really blessed that you're here. Any closing remarks?

Dr. Rubin:
Now, I want to thank you, because the reality is that an effective campaign to raise awareness and improve the health of our community has to do with education and leaders like you who put on programs like this to make sure people understand the facts. And the more we can disseminate facts and celebrate the success of science and demystify it for our patients and, frankly, for other colleagues, the better we'll all be.

Dr. Nandi:
Thank you very much. We're very humbled and very appreciative indeed.

For ReachMD. I'm Dr. Neil Nandi. To access this episode and others from *GI Insights*, please visit ReachMD.com/GIInsights where you can be part of the knowledge. Thanks for listening.