ADVANCES IN IBD

Current Developments in the Treatment of Inflammatory Bowel Disease

Section Editor: Stephen B. Hanauer, MD

Use of Glucagon-Like Peptide-1 Receptor Agonists in Patients With Inflammatory Bowel Disease

Christine Boumitri, MD
Assistant Professor
Feinberg School of Medicine
Northwestern Medicine
Chicago, Illinois

G&H How prevalent are obesity and overweight in patients with inflammatory bowel disease, and how can these conditions affect this patient population?

CB With the global increase in obesity and overweight, a similar trend has been seen in patients with inflammatory bowel disease (IBD), a population historically considered to be malnourished. Recent studies have shown that 15% to 40% of patients with IBD are classified as overweight, whereas approximately 15% to 20% of patients meet the criteria for obesity.

These conditions can impact the course of IBD, including disease activity, patient response to therapy, and surgical outcomes. For instance, obesity has been associated with a chronic low-grade inflammatory status because adipose tissue can release inflammatory cytokines such as interleukin-6 and tumor necrosis factor–alpha, which are also implicated in the pathogenesis of IBD. Another study showed that higher intra-abdominal visceral adipose tissue mass is associated with lower rates of clinical and endoscopic remission in IBD patients initiating biologic therapy.

Obesity can also affect absorption, metabolism, and excretion of drugs, which can sometimes reduce the efficacy of therapy, such as with biologics. This can be seen in clinical practice when providers need to adjust medications based on body weight. In the context of surgical intervention, evidence shows that obese IBD patients face higher risks of postoperative complications, including poor wound healing, prolonged hospitalization, and increased morbidity.

G&H Have studies looked at whether glucagon-like peptide-1 receptor agonists are effective for weight loss specifically in patients with IBD?

CB Recent studies have shown that glucagon-like peptide-1 (GLP-1) receptor agonists are effective for weight loss in IBD patients. A retrospective cohort study published in *Inflammatory Bowel Diseases* assessed patients with obesity and IBD who were prescribed the GLP-1 receptor agonist semaglutide (Novo Nordisk). The findings revealed a mean total body weight reduction of approximately 16 lb, which was comparable with the weight loss observed in patients who did not have IBD. Importantly, this study did not show an increased risk of IBD-specific adverse reactions or events associated with the use of this GLP-1 receptor agonist. Similarly, an observational cohort study investigated the effect of tirzepatide (Lilly) as well as semaglutide in nondiabetic patients with IBD who were prescribed a GLP-1 receptor agonist. The study showed a significant decrease in body mass index and total body weight, with a medium weight loss of 8.15 kg. These findings suggest that GLP-1 receptor agonists can be effective for weight loss in IBD patients.

G&H Have these agents been shown to affect outcomes of patients who have IBD?

CB Recent studies have been looking at the effect of GLP-1 receptor agonists on outcomes in patients with IBD. A study published in *Inflammatory Bowel Diseases* evaluating the impact of GLP-1 receptor agonists on IBD

outcomes found that their use is not associated with an increased rate of IBD exacerbation. This means that these medications can be safely prescribed in the IBD patient population. There was also no change in IBD-related hospitalization, corticosteroid prescription, medication escalation (need to change medication or escalate therapy), or IBD-related surgery.

A poster presented at Digestive Disease Week 2024 by Dr Priya Sehgal and colleagues looked at the safety and efficacy of GLP-1 receptor agonists on weight management in IBD patients as well as the impact of these agents on inflammatory biomarkers. The authors checked baseline C-reactive protein (CRP) and fecal calprotectin at the time of GLP-1 receptor agonist initiation and compared those with CRP and fecal calprotectin 12 to 24 weeks after starting the medications. This study excluded patients who were started on corticosteroids or who had a change in their IBD therapy during the study period. The authors saw a decrease in CRP at 12 to 24 weeks, which was statistically significant, as well as a reduction in fecal calprotectin, although that was not statistically significant.

… there is a suggestion that GLP-1 receptor agonists may have a beneficial effect on IBD outcomes.

Additionally, a recent Danish nationwide cohort study looked at the risk of ileus and intestinal obstruction in patients with IBD who were receiving GLP-1 receptor agonists. It is known that these agents can delay gastric emptying and slow the transit of food. This study found that GLP-1 receptor agonist exposure was not associated with an increased risk of ileus or intestinal obstruction in patients with IBD. This is important for IBD patients who have concerns about the potential gastrointestinal (GI) side effects associated with the use of these agents.

In summary, there is a suggestion that GLP-1 receptor agonists may have a beneficial effect on IBD outcomes. However, more prospective studies are needed to confirm these findings and establish the role of these medications in the management of IBD.

G&H Has the research to date demonstrated any other potential beneficial effects of these drugs on IBD patients?

CB Emerging research suggests that GLP-1 receptor agonists may influence inflammatory pathways in patients with IBD, although the evidence is still evolving. There is a suggestion that GLP-1 receptor agonists have anti-inflammatory properties that might be beneficial in IBD. The effects of GLP-1 receptor agonists were studied in mice with dextran sulfate sodium (DSS)-induced colitis in vivo and in vitro. The results of this study showed that GLP-1 represses the production of proinflammatory mediators and alleviates DSS-induced injury to the intestinal mucosa and dysbiosis of the gut microbiota. Other research has shown that these agents modulate key pathways involved in IBD pathogenesis, such as chronic inflammatory circuits, the gut microbiome, dysbiosis, and intestinal tight junctions.

Patients with IBD also often experience metabolic complications, including obesity and type 2 diabetes, and GLP-1 receptor agonists are effective in improving glycemic control and promoting weight loss, which can be advantageous for IBD patients who have these comorbidities. By addressing metabolic dysfunction, these agents may be contributing to overall disease management and improving these particular patient population outcomes.

Additionally, IBD patients are at increased risk of cardiovascular disease, and GLP-1 receptor agonists have been shown to reduce cardiovascular events in patients with type 2 diabetes by mechanisms that include the inflammatory pathway. Perhaps similar benefits may extend to IBD patients that can potentially lower their cardiovascular risk as well. This research highlights the benefits of GLP-1 receptor agonists and the promise of using them as adjunct therapy in IBD management, particularly for patients with coexisting obesity and metabolic syndrome.

G&H Which side effects have been reported with the use of these agents in IBD patients?

CB GLP-1 receptor agonists are commonly associated with GI side effects. The side effects most commonly experienced are nausea, vomiting, changes in bowel habits (whether diarrhea or constipation), and abdominal pain. These symptoms are usually mild to moderate, and tend to subside over time. IBD patients may already be experiencing these symptoms, so providers should monitor these patients carefully because the use of GLP-1 receptor agonists might exacerbate these preexisting symptoms.

There had been initial concern that GLP-1 receptor agonist use could be associated with an increased risk of pancreatitis. However, we do not have studies confirming that there is a significant association. Nevertheless, providers should be cautious when prescribing GLP-1 receptor agonists if patients have a history of pancreatitis.

Additionally, there have been reports of worsening chronic kidney failure or acute kidney injury in patients who are using GLP-1 receptor agonists. Some IBD patients experiencing significant diarrhea can be at higher risk of dehydration when using these drugs. Physicians have to select the right patient population for these medications, and gradual dose titration can help mitigate GI symptoms.

G&H Have there been any concerns with the use of these agents in conjunction with advanced IBD therapies?

CB GLP-1 medications do not have significant direct interaction with the most commonly used IBD medications such as corticosteroids, immunomodulators, and biologics. However, GLP-1 receptor agonists can sometimes affect absorption because they can impact the gastric emptying of certain medications. It is crucial to consider the medications that patients are taking and look for potential direct or indirect interactions.

G&H Are there any limitations to the use of GLP-1 receptor agonists in IBD patients?

CB Although GLP-1 receptor agonists show potential benefit in IBD patients, the decision to use these agents should be individualized owing to the risk of potential GI side effects overlapping with IBD symptoms, which can make symptom management more complex. We have limited data on long-term safety, and we need more clinical trials to evaluate their long-term effects in IBD patients. Physicians have to ensure that patients do not have an underlying motility disorder such as gastroparesis, which might worsen with the use of these drugs. As our experience with using these medications in IBD patients increases over the years, it will be important to stay informed about any potential side effects, as it may take years for certain effects to be seen.

G&H What misconceptions have you seen about GLP-1 receptor agonist use in the IBD population?

CB Some physicians are reluctant to prescribe these medications to patients with IBD. It is important to look at the studies done so far, which show that these medications can be safe and may be beneficial when selecting the right patient. There is a misconception that GLP-1 receptor agonists may negatively interact with biologics and immunosuppressants. The current evidence does not indicate a significant adverse interaction between these drugs.

G&H What are the priorities of research?

CB Prospective studies are needed to confirm the role of GLP-1 receptor agonists in directly altering the inflammatory pathway in patients with IBD and how these drugs affect intestinal epithelial integrity as well as the microbiome. We also need more research to determine whether GLP-1 receptor agonists have differential effects on Crohn's disease vs ulcerative colitis. Additionally, large-scale studies are needed to assess the long-term safety and tolerability of these drugs in IBD patients.

Disclosures

Dr Boumitri has no relevant conflicts of interest to disclose.

Suggested Reading

Desai A, Khataniar H, Hashash JG, Farraye FA, Regueiro M, Kochhar GS. Effectiveness and safety of semaglutide for weight loss in patients with inflammatory bowel disease and obesity [published online April 20, 2024]. *Inflamm Bowel Dis*. doi:10.1093/ibd/izae090.

Gorelik Y, Ghersin I, Lujan R, et al. GLP-1 analog use is associated with improved disease course in inflammatory bowel disease: a report from the Epi-IIRN [published online October 23, 2024]. *J Crohns Colitis*. doi:10.1093/ecco-jcc/jjae160.

Harper JW, Sinanan MN, Zisman TL. Increased body mass index is associated with earlier time to loss of response to infliximab in patients with inflammatory bowel disease. *Inflamm Bowel Dis*. 2013;19(10):2118-2124.

Levine I, Sekhri S, Schreiber-Stainthorp W, et al. GLP-1 receptor agonists confer no increased rates of IBD exacerbation among patients with IBD [published online October 22, 2024]. *Inflamm Bowel Dis*. doi:10.1093/ibd/izae250.

Nic Suibhne T, Raftery TC, McMahon O, Walsh C, O'Morain C, O'Sullivan M. High prevalence of overweight and obesity in adults with Crohn's disease: associations with disease and lifestyle factors. *J Crohns Colitis*. 2013;7(7):e241-e248.

Nielsen J, Friedman S, Nørgård BM, Knudsen T, Kjeldsen J, Wod M. Glucagon-like peptide 1 receptor agonists are not associated with an increased risk of ileus or intestinal obstruction in patients with inflammatory bowel disease—a Danish nationwide cohort study [published online November 27, 2024]. *Inflamm Bowel Dis*. doi:10.1093/ibd/izae276.

Singh S, Dulai PS, Zarrinpar A, Ramamoorthy S, Sandborn WJ. Obesity in IBD: epidemiology, pathogenesis, disease course and treatment outcomes. *Nat Rev Gastroenterol Hepatol*. 2017;14(2):110-121.

St-Pierre J, Klein J, Choi NK, Fear E, Pannain S, Rubin DT. Efficacy and safety of GLP-1 agonists on metabolic parameters in non-diabetic patients with inflammatory bowel disease. *Dig Dis Sci*. 2024;69(12):4437-4445.

Wang W, Zhang C, Zhang H, Li L, Fan T, Jin Z. The alleviating effect and mechanism of GLP-1 on ulcerative colitis. *Aging (Albany NY)*. 2023;15(16):8044-8060.

Weidinger C, Ziegler JF, Letizia M, Schmidt F, Siegmund B. Adipokines and their role in intestinal inflammation. *Front Immunol*. 2018;9:1974.

Yarur AJ, Bruss A, Moosreiner A, et al. Higher intra-abdominal visceral adipose tissue mass is associated with lower rates of clinical and endoscopic remission in patients with inflammatory bowel diseases initiating biologic therapy: results of the Constellation study. *Gastroenterology*. 2023;165(4):963-975.e5.