An Antiemetic for Irritable Bowel Syndrome?

A drug used for cancer patients may provide some relief to patients with IBS.

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PRACTICE CHANGER

Consider prescribing ondansetron (up to 24 mg/d) for patients who have irritable bowel syndrome with diarrhea (IBS-D).[1]

STRENGTH OF RECOMMENDATION

B: Based on a well-done double-blind, placebo-controlled randomized controlled trial (RCT).[1]

ILLUSTRATIVE CASE

A 23-year-old woman who was diagnosed with irritable bowel syndrome (IBS) comes to your clinic with complaints of increased frequency of defecation with watery stools and generalized, cramping abdominal pain. She also notes increased passage of mucus and a sensation of incomplete evacuation.

She says the only thing that relieves her pain is defecation. She has tried loperamide, acetaminophen, and ibuprofen without relief. She does not have Crohn disease or ulcerative colitis. What else can you offer her that is safe and effective?

IBS is a chronic, episodic functional gastrointestinal disorder characterized by abdominal pain or discomfort and altered bowel habits: constipation (IBS-C), diarrhea (IBS-D), or alternating periods of both—mixed (IBS-M).[2] The diagnosis is based on Rome III criteria, which include recurrent abdominal pain or discomfort on at least three days per month in the past three months associated with two or more of the following: improvement with defecation, onset associated with a change in frequency of stool, and onset associated with a change in form (appearance) of stool.[3] IBS often is unrecognized or untreated, and as few as 25% of patients with IBS seek care.[4]

IBS-D affects approximately 5% of the general population in North America.[5,6] IBS-D is associated with a considerably decreased quality of life and is a common cause of work absenteeism.[7,8] Because many conditions can cause diarrhea, patients typically undergo numerous tests before receiving an accurate diagnosis, which creates a financial burden.[9]

For many patients, current IBS treatments—including fiber supplements, laxatives, antidiarrheal medications, antispasmodics, and antidepressants such as tricyclics and selective serotonin reuptake inhibitors—are unsatisfactory.[10] Alosetron, a 5-hydroxytryptamine 3 (5-HT3) receptor antagonist, has been used to treat IBS-D,[11] but this medication was voluntarily withdrawn from the US market in 2000 due to concerns about ischemic colitis and severe constipation.[12] It was reintroduced in 2002 but can be prescribed only by clinicians who enroll in a prescribing program provided by the manufacturer, and there are restrictions on its use.

Ondansetron—another 5-HT3 receptor antagonist used to treat nausea and vomiting caused by chemotherapy—may be another option for treating IBS-D. Garsed et al[1] recently conducted an RCT to evaluate the efficacy of ondansetron for patients with IBS-D.

STUDY SUMMARY

Ondansetron improves stool consistency, severity of IBS symptoms

In a five-week, double-blind crossover RCT, Garsed et al[1] compared ondansetron with placebo for symptom relief in 120 patients who met Rome III criteria for IBS-D. All patients were ages 18 to 75 and had no evidence of inflammatory bowel disease. Exclusion criteria included pregnancy or breastfeeding, unwillingness to stop antidiarrheal medication, prior abdominal surgery other than appendectomy or cholecystectomy, or enrollment in another trial.

Patients were started on ondansetron 4 mg/d with dose titration up to 24 mg/d based on response; no dose adjustments were allowed during the last two weeks of the study. There was a two- to three-week washout between treatment periods.

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The primary endpoint was average stool consistency in the last two weeks of treatment, as measured by the Bristol Stool Form (BSF) scale.[13] The BSF is a visual scale that depicts stool as hard (type 1) to watery (type 7); types 3 and 4 describe normal stools. The study also looked at urgency and frequency of defecation, bowel transit time, and pain scores.

Treatment with ondansetron resulted in a small but statistically significant improvement in stool consistency. The mean difference in BSF score between ondansetron and placebo was –0.9, indicating slightly more formed stool with use of ondansetron. Scores for IBS severity—mild (a score of 75 to 175 out of 500), moderate (175 to 300), or severe (> 300)—were reduced by more points with ondansetron than with placebo (83 ± 9.8 vs 37 ± 9.7, respectively). Although this mean difference of 46 points fell just short of the 50-point threshold that is considered clinically significant, many patients exceeded this threshold.

Compared to those who received placebo, patients who took ondansetron also had less frequent defecation and lower urgency scores. Gut transit time was lengthened in the ondansetron group by 10 hours more than in the placebo group.

Pain scores did not change significantly for patients taking ondansetron, although they experienced significantly fewer days of urgency and bloating. Symptoms typically improved in as little as seven days but returned after ondansetron use stopped (typically within two weeks). Sixty-five percent of patients reported adequate relief with ondansetron, compared to 14% with placebo.

Patients whose diarrhea was more severe at baseline didn't respond as well to ondansetron as did those whose diarrhea was less severe. The only frequent adverse effect was constipation, which occurred in 9% of patients receiving ondansetron and 2% of those on placebo.

> *"Ondansetron should not be prescribed to IBS patients who experience constipation or those with mixed symptoms."*

WHAT'S NEW

Another option for IBS-D

A prior, smaller study of ondansetron that used a lower dosage (12 mg/d) suggested benefit in IBS-D.[14] In that study, ondansetron decreased diarrhea and functional dyspepsia. The study by Garsed et al[1] is the first large RCT to show significantly improved stool consistency, less frequent defecation, and less urgency and bloating from using ondansetron to treat IBS-D.

CAVEATS

Ondansetron doesn't appear to reduce pain

In Garsed et al,[1] patients who received ondansetron did not experience relief from pain, which is one of the main complaints of IBS. However, this study did find slight improvement in formed stools, symptom relief that approached—but did not quite reach—clinical significance, fewer days with urgency and bloating, and less frequent defecation.

This study did not evaluate the long-term effects of ondansetron use. However, ondansetron has been used for other indications for more than 25 years and has been reported to have a low risk for adverse effects.[15]

CHALLENGES TO IMPLEMENTATION

Remember ondansetron is not for IBS patients with constipation

Proper use of this drug among patients with IBS is key. The primary benefits of ondansetron are limited to IBS patients who have diarrhea, and not constipation. Ondansetron should not be prescribed to IBS patients who experience constipation or those with mixed symptoms. **CR**

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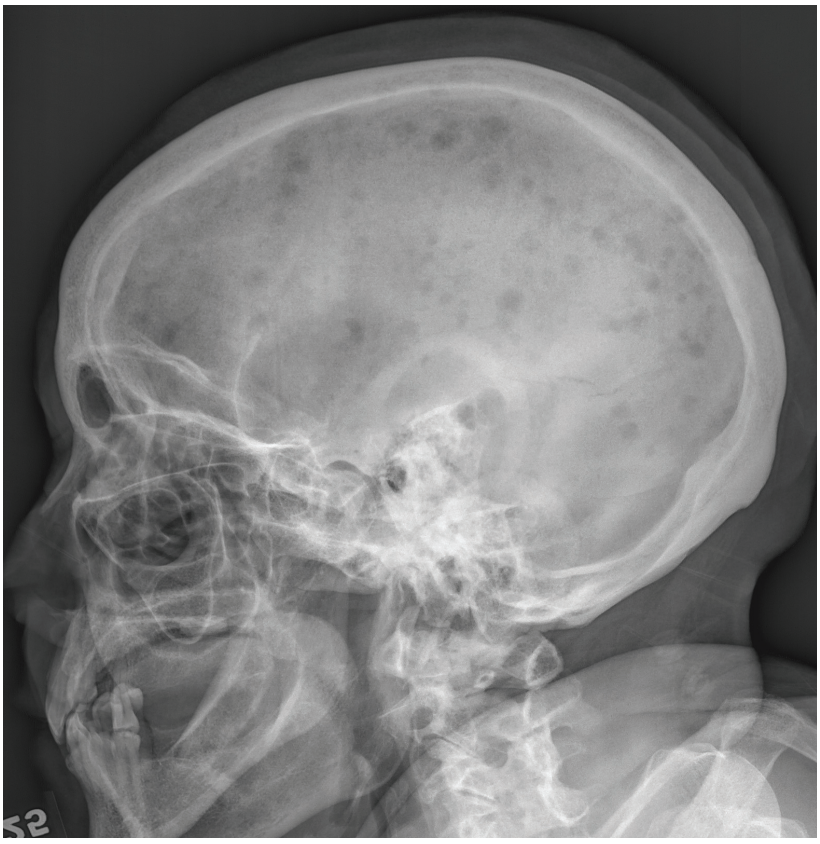

ANSWER

The radiograph demonstrates innumerable small lytic defects throughout the calvarium. The patient's confusion is most likely secondary to profound metabolic abnormalities. However, in the setting of lytic bone lesions, metabolic abnormalities of renal insufficiency, severe hypercalcemia, and hypomagnesemia, one must be concerned about an occult myeloma, and appropriate work-up must be done. **CR**

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