

THE EFFECTIVE PHYSICIAN

Gastroparesis

BY WILLIAM E. GOLDEN, M.D., AND ROBERT H. HOPKINS, M.D.

Background

Patients with gastroparesis present numerous challenges to the practicing internist. The American Gastroenterological Association recently released recommendations on the diagnosis and treatment of this condition.

Conclusions

Gastroparesis is a symptomatic, chronic disorder of delayed gastric emptying, without mechanical obstruction. Patients typically have nausea and vomiting, early satiety, bloating, and upper abdominal pain. Common causes include diabetes, postsurgical changes, and idiopathic presentations. In diabetes, gastroparesis can reflect neuropathy of the vagus nerve or impaired motility secondary to hyperglycemia. As many as 20%-40% of diabetic patients eventually develop symptoms of gastroparesis.

Gastroparesis can occur as a complication after laparoscopic fundoplication for gastroesophageal reflux disease. It is also seen with vagal denervation of the stomach after pyloroplasty. Gastrojejunostomy with distal gastric resection can result in severe gastric stasis and/or delayed small bowel transit in the denervated efferent loop. Idiopathic gastroparesis is seen mostly in women. Some evidence suggests a viral etiology in a subset of these patients, who typically have a slow resolution of symptoms over several years.

Gastroparesis should be distinguished from the cyclical vomiting syndrome, which is characterized by episodes of relentless nausea and vomiting lasting hours to days and sometimes associated with migraine headaches.

Diagnosis

► Scintigraphy is the gold standard for diagnosis. Such studies require assessment of the emptying of solids; emptying of liquids may be normal even in severe gastroparesis. The radiolabel must be cooked into a test meal to ensure binding to the solid phase. Scintigraphy should be extended to at least 2-4 hours.

► The upper GI barium series is insensitive for measuring gastric emptying, as barium is not a physiologic test meal.

► Patients should stop drugs that could affect gastric emptying for at least 48-72 hours prior to a study. Opiate analgesics and anticholinergic agents can delay emptying. Serotonin receptor antagonists, such as ondansetron, do not affect emptying and can be continued. Other drugs that can delay gastric emptying include tricyclic antidepressants, calcium channel blockers, progesterone, proton pump inhibitors, diphenhydramine, and L-dopa, as can alcohol.

Treatment

► Treatment should focus on correcting fluid and electrolyte abnormalities, improving underlying conditions, and reducing symptoms.

► Dietary recommendations include eating small, frequent meals; increasing fluids; and reducing fat and fiber intake. Carbonated beverages can aggravate gastric distention. Alcohol and tobacco products impair gastric function.

► Maintaining euglycemia in patients with diabetes can improve gastric motor function as well as the effects of prokinetic agents.

► Antiemetic agents are a primary therapy. Phenothiazines act on the area postrema of the

medulla oblongata. Serotonin (5-HT³) receptor antagonists may act on the area postrema and the afferent branches of the vagus nerve. Although 5-HT³ agents are effective in other causes of nausea and vomiting, no studies document the efficacy of these drugs for gastroparesis.

► There is little evidence that antihistamines are effective for symptom control of gastroparesis. Transdermal hyoscine (the scopolamine patch) may actually delay gastric emptying.

► Prokinetic agents can increase antral contractility, improve gastric muscle function, and improve antroduodenal coordination. Some agents, such as metoclopramide and domperidone, have antiemetic properties. Response to these medications is judged clinically, rather than with follow-up gastric emptying tests.

► Metoclopramide, used for 35 years to treat gastroparesis, has prokinetic and antiemetic actions. The dosage can be increased to 20 mg before meals and at bedtime, especially for patients with severe symptoms. A small subset of patients can have acute dystonic reactions. Prolonged use of metoclopramide can produce parkinsonian-like symptoms, which usually subside 2-3 months after discontinuation. Tardive dyskinesia is seen in up to 15% of patients on higher doses for at least 3 months.

► Domperidone doesn't cross the blood-brain barrier and has fewer extrapyramidal effects than metoclopramide. In one study, its effect on solid-phase emptying was lost after 6 weeks.

► Erythromycin can stimulate gastric emptying in diabetic gastroparesis, idiopathic gastroparesis, and postvagotomy conditions. It may be most potent when used intravenously. Oral administration should start at low doses, such as 125-250 mg three to four times daily; liquid suspensions can improve absorption. Intravenous erythromycin, 100 mg every 8 hours, is used for patients hospitalized with severe conditions.

► Three-quarters of patients with refractory gastroparesis in one study responded to a prokinetic agent, but up to one-quarter were refractory to all interventions. If all pharmacotherapy fails, consider placement of a feeding jejunostomy and/or venting gastrostomy.

► New therapies under evaluation include injection of botulinum toxin into the pyloric region and gastric electric stimulation.

Reference

Parkman H.P., et al. American Gastroenterological Association Technical Review on the Diagnosis and Treatment of Gastroparesis. *Gastroenterology* 2004;127:1592-622.



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'Prebiotic' May Hold Promise for Crohn's

BY ANN C. LOGUE
Contributing Writer

CHICAGO — Ten patients with moderate Crohn's disease took supplements of fructooligosaccharide, a substance found in artichokes and asparagus, and showed an increase in fecal *Bifidobacteria* and production of mucosal dendritic cells, James Lindsay, Ph.D. reported at the Digestive Disease Week.

Although the findings are preliminary, this is the first known study of "prebiotic" dietary therapies for Crohn's, and the strategy may offer a way to supplement traditional treatments or to manage patients who do not respond to them, he said.

Fructooligosaccharide is a carbohydrate that selectively alters the colonic microbiota, Dr. Lindsay explained. It is a prebiotic that may provide a substrate upon which healthy bacteria can grow, as opposed to probiotics, which are the healthy bacteria themselves.

The supplement given to the 10 patients in the open-label study was prepared by Nestlé UK, which provided financial support for the research. The patients took 15 g per day for 3 weeks.

Patients and doctors noted an improvement on the Harvey Bradshaw index, with the mean falling from 9.8 at the start of the study to 6.9 at the end. Remission of

Crohn's disease was achieved by 40% of the patients. There was a 6.8% increase in the volume of *Bifidobacteria* found in dried fecal samples between the start and end of the study. In addition, the number of interleukin-10 dendritic cells increased, as did the number of cells expressing Toll-like receptors.

Patients in the study, 60% of whom were completely compliant with the study regimen, tolerated the supplement well. The most common complaints were rumbling and flatulence.

"Traditional therapies tend to increase effector pathways. The alternative is to increase regulatory pathways," said Dr. Lindsay, consultant gastroenterologist at St Bartholomew's Hospital and the Royal London Hospital.

Balfour Sartor, M.D., a professor of medicine, microbiology, and immunology at University of North Carolina at Chapel Hill, is familiar with the work of Dr. Lindsay and his colleagues because it overlaps with his own. He said that Dr. Lindsay's study is not in the mainstream of Crohn's research, but that it is a legitimate area of investigation.

Dr. Lindsay emphasized the preliminary nature of the findings. "One would have to be quite cautious in interpreting the results until we have performed a controlled trial," he said. ■

In Japan, Crohn's Disease Rises As Rice Consumption Falls

CHICAGO — The increasing prevalence of Crohn's disease in Japan correlates closely with the decreasing consumption of rice, Ryosuke Shoda, M.D., said at the annual Digestive Disease Week.

Crohn's disease was once almost unknown in Japan, Dr. Shoda said in a poster presentation. In the early 1960s and before, rice was the main source of dietary fiber in Japan, providing the average citizen with about 28 g of fiber per day. Today, the average intake of fiber from rice is 12-15 g/day.

Meanwhile, the prevalence of Crohn's disease went from virtually nothing in the 1960s to 2.9 per 100,000 persons in the mid-1980s and about 14 per 100,000 today, said Dr. Shoda, chief of the department of general internal medicine at the International Medical Center of Japan, Tokyo.

Data on fiber consumption and Crohn's disease from the Japanese Ministry of Health, Welfare, and Labor from 1966 to 1993 show

that the rising prevalence of Crohn's disease closely paralleled the decreasing intake of fiber and rice and the increasing intake of fiber from wheat and grains, Dr. Shoda said.

Of nine sources of fiber studied, rice was the only one that was independently correlated with the prevalence of Crohn's disease. When changes in the consumption of animal fat were included in the analysis, rice remained the only independent factor.

Breakfast is the meal that has changed the most in Japan and is probably the most responsible for the decline in rice consumption, Dr. Shoda said in an interview. Many people in Japan now eat bread rather than rice with breakfast.

Dr. Shoda declined to speculate on what might explain the association. "This is just statistics," he told this newspaper. "No one knows about this for certain. There must be other factors."

—Timothy F. Kirn