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Diagnosis, Treatment and Nutritional Management of Chronic Intestinal Pseudo-Obstruction

Brian E. Lacy

Burr J. Loew

Chronic intestinal pseudo-obstruction (CIP) is a rare, chronic disorder of the luminal gastrointestinal tract. Symptoms and signs suggest a mechanical bowel obstruction, although in the evaluation of patients with CIP, both routine and specialized tests fail to identify evidence of mechanical obstruction. Common symptoms include nausea, vomiting, bloating, abdominal distension, and involuntary weight loss. Unfortunately, these symptoms are non-specific, frequently leading to either misdiagnosis or a delay in diagnosis. Many patients require parenteral nutrition and a large number of patients require chronic opioids. This review will focus on the etiology, pathogenesis, diagnosis and treatment of patients with CIP.

INTRODUCTION

Chronic intestinal pseudo-obstruction (CIP) is a rare and potentially life-threatening disorder of the gastrointestinal tract characterized by symptoms and signs suggestive of mechanical obstruction but in the absence of a true anatomical lesion. Normal antegrade propulsive activity of the gastrointestinal tract is defective in CIP; when significant, chronic intestinal failure ensues with an inability to maintain normal weight and achieve adequate nutrition. This disease entity typically goes unrecognized for long periods of time before the correct diagnosis is established. In the interim, patients often undergo repeated and potentially dangerous tests and treatments. This monograph will focus on the following aspects of CIP: understanding the impact of intestinal pseudo-obstruction; describing the etiology and pathophysiology of CIP; reviewing common symptoms and signs; discussing the accurate diagnosis of CIP; and finally, reviewing treatment options.

Brian E. Lacy, Ph.D., M.D. FACG, Associate Professor of Medicine, Dartmouth Medical School, Director, GI Motility Laboratory, Dartmouth-Hitchcock Medical Center, Lebanon, NH. Burr J. Loew, M.D., Fellow in Gastroenterology, Division of Gastroenterology and Hepatology, Dartmouth-Hitchcock Medical Center, Lebanon, NH.

CASE 1

DB is a 43-year-old woman referred for further evaluation of abdominal pain, nausea, vomiting, and weight loss. Her past medical history was notable for an episode of volvulus 10 years earlier that required right hemi-colectomy. After surgery, she had alternating symptoms of constipation and diarrhea and was labeled with the diagnosis of irritable bowel syndrome (IBS). Two years ago she had a viral illness with symptoms of nausea, vomiting, diarrhea, fever, myalgias and arthralgias. All of the symptoms except for her nausea and vomiting resolved. Her weight dropped from 100 to 70 lbs. She noticed difficulty swallowing liquids and solids. She denied symptoms of anorexia and bulimia, believed that her weight was too low, and did not exercise. Physical examination revealed a cachectic woman with a BMI of 13.3. Her abdomen was moderately distended and tympanitic. Blood tests were notable for an albumin of 2.2; her electrolytes were normal as was a TSH. Her hemoglobin was 10 with a normal MCV. She was evaluated by multiple physicians and underwent a variety of diagnostic tests:

- Two separate upper endoscopies were normal
- Two separate colonoscopies revealed a patent anastomosis without evidence of obstruction
- An abdominal flat plate while acutely ill showed dilated loops of small intestine with multiple air fluid levels
- A follow-up abdominal x-ray two weeks later appeared normal
- A right upper quadrant ultrasound showed evidence of prior cholecystectomy but was otherwise normal
- Two separate computed tomography (CT) scans of the abdomen and pelvis were normal other than demonstrating post-surgical changes
- A small bowel follow-through did not show evidence of obstruction however transit was delayed at four hours
- Extensive blood tests, looking for evidence of a connective tissue disorder or autoimmune disorder, were all normal
- An MRI of the brain was normal as well
- Esophageal manometry revealed normal lower esophageal sphincter (LES) resting pressure of 17 mm Hg and complete LES relaxation, but failed peristalsis on nine of 10 water swallows. One swallow was peristaltic in nature and of normal amplitude
- The four hour solid phase gastric emptying scan revealed 27% of material remaining at four hours (<10% = normal)
- Antroduodenal manometry revealed antral hypomotility, absence of a spontaneous MMC, minimal response in the stomach to intravenous erythromycin (50 mg) without generation of a Phase III activity front, minimal response to octreotide (50 micrograms) in the small intestine, and a blunted fed response to a standard meal

These findings were felt to be most consistent with a neuropathic process involving the esophagus, stomach, and proximal small intestine. The patient was started on TPN; however her liver tests became markedly elevated prompting discontinuance. A J-tube was placed surgically and a full-thickness small bowel biopsy revealed normal circular and longitudinal muscle, but absent ganglion cells and disordered nerve terminals. The diagnosis of chronic intestinal pseudo-obstruction (CIP) of the neuropathic type was made. The patient was started on J-tube feedings and treated with antiemetics and low dose opioids with a slow return of weight to 90 lbs over a 12-month period.

CASE 2

GP is a 55-year-old man sent for a second opinion in gastroenterology due to symptoms of nausea, vomiting, bloating, and diarrhea. He states that his symptoms began approximately seven years ago. His weight at that time was 145 lbs. He does not recall any specific precipitating event, but noted the gradual onset of bloating and diarrhea. He was told that he had lactose intolerance, although avoiding all dairy products did not seem to help. He was given the diagnosis of IBS and was advised to use loperamide on a p.r.n. basis. This helped his diarrhea somewhat, although he still had significant bloating. A low fiber diet did not improve his bloating symptoms. Over the next two-to-three years he noticed the gradual onset of nausea and vomiting. During the next several years he developed new symptoms of pyrosis and dysphagia. He was

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treated with an over-the-counter PPI with some relief of heartburn symptoms but no relief of dysphagia. His internist became concerned when he returned for a follow-up visit and his weight was 117 lbs. Diagnostic workup revealed the following:

- Laboratory tests were performed (CBC, ESR, electrolytes, BUN/Cr, glucose, LFTs, serum TTG antibody, serum IgA) and all returned normal
- Colonoscopy, including random biopsies, was normal
- Upper endoscopy, including random biopsies of the duodenum and stomach, were normal
- A small bowel follow through revealed slow transit (five hours) through a moderately dilated small intestine. There was no evidence of obstruction
- A laboratory panel for autoimmune disorders or connective tissue disorders was obtained (ANA, AMA, anti-smooth muscle antibody, CRP, TSH, SCL-70 panel, anti-double stranded DNA, anti-Hu antibody, SPEP). ANA was elevated at a titer of 1:1500, but labs were otherwise normal
- Esophageal manometry revealed a hypotensive LES with resting pressure of 2 mm Hg, normal UES resting pressure and relaxation, but absent peristalsis in the body of the esophagus
- A four-hour solid phase gastric emptying scan was delayed with 37% of the material remaining at four hours (normal <10%)
- A double-contrast barium enema revealed a markedly dilated, redundant colon. More than three liters of barium was used to coat the colon
- Antroduodenal manometry revealed very low amplitude contractions in the antrum (15–20 mm; normal up to 250 mm Hg), a spontaneous MMC that originated in the stomach, although it was of very low amplitude; barely perceptible contractions in the small intestine but of normal frequency (13 cpm), and minimal response to erythromycin in the stomach and octreotide in the small intestine
- The lactulose hydrogen breath test was positive for bacterial overgrowth with an elevated hydrogen level at baseline and an early peak of breath hydrogen.

He described having 20-to-30 loose, non-bloody bowel movements each day and generalized abdominal pain not relieved with over-the-counter analgesics. His BMI was 22.7. His pulse was 78 and regular with a blood pressure of 134/74. His physical examination was noted for muscle wasting in the temporal region and supraclavicular regions bilaterally. His abdomen was markedly distended and tympanitic. He had mild diffuse abdominal tenderness without rebound or guarding. His liver was normal in size on palpation; the spleen could not be palpated. The symptoms of dysphagia, nausea, vomiting, bloating, distention and diarrhea with a dilated small intestine raised the issue of a generalized neuromuscular disorder of the gastrointestinal tract. Based on these tests the patient was diagnosed with CIP of the myopathic origin. He was placed on a liquid diet, treated with antibiotics for bacterial overgrowth, and scheduled for exploratory laparoscopy with full thickness biopsy to confirm the diagnosis. Unfortunately, before he could have his surgery, he developed an episode of bowel obstruction diagnosed as colonic volvulus. He underwent near total colectomy with colostomy at his local hospital. A Mediport was placed at the same time and the patient was started on TPN. The pathology specimens revealed atrophy of the smooth muscle layers in the colon, consistent with hollow visceral myopathy. Ganglion cells were present. The patient has remained on TPN and has slowly gained weight. Rotating antibiotics have been used to treat chronic small bowel bacterial overgrowth and symptoms of bloating and distention with some relief.

THE IMPACT OF CHRONIC INTESTINAL PSEUDO-OBSTRUCTION

Chronic intestinal pseudo-obstruction was first described in 1958 after a number of patients who had symptoms suggestive of a mechanical bowel obstruction had normal findings at the time of exploratory surgery (1). The exact prevalence of CIP remains unknown, although it is estimated that approximately 100 infants are born with congenital pseudo-obstruction each year in the United States (2). This number, however, significantly underestimates the total number of new cases each year, as it does not include the large cohort of adult patients who develop intestinal pseudo-obstruction later in life. The economic cost to society, including days missed from work or school, physician visits, diagnostic testing, hospital admissions, and unnecessary procedures, is unknown.

Schwankovsky and co-workers published quality of life measurements after a retrospective review of the medical records of 58 patients with congenital CIP (3). Their results demonstrate that a large number of CIP patients (73%) require central venous access or a percutaneous gastrostomy tube in order to maintain adequate nutrition. Furthermore, children with CIP, compared to healthy children, had lower levels of self-care and mobility, more difficulty attending school and participating in social activities, and more pain, anxiety and depression. Parents of children with CIP had an emotional status rated as "poor" when compared to parents of healthy children.

The quality of life for adults with intestinal pseudo-obstruction has not been well studied in a prospective manner, although it is undoubtedly worse than the general population and patients with many other chronic disorders. In one published report, Mann and colleagues described CIP patients as frequently being dependent upon supplemental intravenous or enteral nutrition (EN), using multiple expensive medications (often without success), and often becoming dependent on narcotics due to chronic abdominal pain further aggravating the pseudo-obstruction symptoms (4).

IDENTIFYING THE CAUSE AND MECHANISM OF DISEASE

Chronic intestinal pseudo-obstruction is generally grouped into three categories: primary (either neuropathic or myopathic in nature); secondary (due to systemic disorders including collagen vascular diseases, endocrine disorders, malignancies, neurologic disorders, etc.); or idiopathic (cause unknown). Table 1 depicts this classification system and also lists conditions commonly associated with CIP.

Normal gastrointestinal motor function is a complex sequence of events with an interplay between numerous physiological inputs that remain poorly understood. Factors critical to normal gastrointestinal tract function include: intact extrinsic innervation from the brain and spinal cord; an intact enteric nervous system; the presence of normally functioning smooth muscle; and normal levels of appropriate gastrointestinal hormones and neurotransmitters. Disruption at any point along this complex physiological network may lead to signs and symptoms suggestive of CIP. It is thus easy to understand how CIP encompasses such a wide spectrum of distinct and variable disease processes with differing pathophysiological mechanisms.

The unifying characteristic of CIP is disordered gastrointestinal tract motility. In primary CIP, which encompasses the majority of cases, this may stem from an inherent defect in the normal mechanisms that control gastrointestinal tract motility, for example, either injury to the smooth muscle (a myopathic process) or to the nervous system (a neuropathic process). Damage to the nervous system in patients with CIP typically involves injury to the enteric nervous system, although injury may also occur to the autonomic nervous system (either the sympathetic or parasympathetic nerves). In addition, within each major group (neuropathic or myopathic) CIP can also be categorized into one of three subcategories: congenital, familial (presumably genetic in nature), or sporadic. Familial visceral myopathy can be further grouped into type 1 (autosomal dominant), type 2 (autosomal recessive with associated ptosis and ophthalmoplegia), or type 3 (autosomal recessive with the presence of gastrointestinal tract dilation). These subcategories may then be further classified to represent areas of intestinal involvement (i.e., colon, small intestine, stomach, esophagus or a combination of all four).

A thorough investigation is needed in patients being evaluated for CIP, as a secondary cause that may be amenable to directed therapies can be identified in some cases. Typical etiologies in this subgroup include collagen vascular disorders, endocrine disorders, neurologic disorders, and medications (Table 1). One of the more common collagen vascular diseases to be associated with CIP is primary systemic sclerosis, which may precede the diagnosis of CIP by several years. Other secondary causes of intestinal pseudo-obstruction include amyloidosis and small cell carcinoma of the lung presenting as a paraneoplastic phenomena (5). Viruses have also been implicated as a possible causative factor in CIP (6).

CLINICAL PRESENTATION

An analysis by Mann and colleagues found that the median age of symptom onset was 17 years with a range of two weeks to 59 years (4). The frequency and sever-

Table 1
Classification of Chronic Intestinal Pseudo-Obstruction

Primary	Secondary	Idiopathic **
I. Myopathic	Collagen Vascular Disease	
A. Congenital	• Primary Systemic Sclerosis	
B. Familial	• Systemic Lupus Erythematosus	
C. Sporadic	• Dermatomyositis/Polymyositis	
	• Periarteritis nodosa	
II. Neuropathic	• Mixed connective tissue disorder	
A. Congenital	• Rheumatoid Arthritis	
B. Familial		
C. Sporadic	Endocrine Disorders	
	• Hypothyroidism/hypoparathyroidism	
	• Diabetes mellitus	
	Neurological Disorders	
	• Parkinson's Disease	
	• Hirschsprung's Disease	
	• Chagas' Disease	
	• Intestinal Hypoganglionosis	
	Drug-Associated	
	• Tricyclic antidepressants	
	• Anticholinergic agents	
	• Ganglionic blockers	
	• Anti-parkinsonian agents	
	• Phenothiazines	
	• Clonidine	
	Miscellaneous*	

*Miscellaneous processes may include: celiac disease, infiltrative diseases (amyloid, lymphoma), neoplastic, familial dysautonomia, metabolic (hypokalemia, hypomagnesemia, hypophosphatemia), jejunoileal bypass, mesenteric vascular insufficiency, alcoholism, viral infections, radiation, post-organ transplant.
**Unknown etiology without known precipitant and unrevealing biopsies for a primary mechanism

ity of symptoms varies remarkably from patient to patient depending upon the location and the extent of the gastrointestinal tract involved (Table 2). The most common symptoms include pain (80%), nausea and vomiting (75%), constipation (40%), and diarrhea (intestinal stasis which promotes bacterial overgrowth; 20%) (7). The clinical picture tends to be dominated by abdominal pain and distension which are particularly severe during episodes of pseudo-obstruction. While the pain may be intermittent and occur only during an acute episode or crisis, typically it is chronic in nature. The pain can be located anywhere in the abdomen, depending upon the extent and location of the involved segment of gastrointestinal tract. Pain typically worsens as bloating and abdominal distension progresses and improves as the crisis resolves.

When the esophagus is involved, decreased esophageal motility and reduced lower esophageal sphincter (LES) tone may lead to complaints of dysphagia, chest pain and reflux symptoms.

Patients with CIP may also develop problems outside of the intestinal tract. The most common extraintestinal manifestation is genitourinary involvement (7), which presents as dilation of the ureter or abnormal bladder function, and commonly leads to complaints of difficulty urinating (8).

Natural History

Two studies have investigated congenital CIP in children presenting within the first year of life and have demonstrated that 60%–80% require parenteral nutrition (PN) and 10%–25% die before adulthood (9,10). Most of the adult data is limited to case reports or small case series so the natural history remains largely unknown. A recent prospective study by Stanghellini and colleagues followed 59 consecutive CIP patients for a median of 4.6 years (11). The diagnosis of CIP was made a median of eight years after symptoms first developed. During this time each patient underwent an average of three surgeries related to their CIP diagnosis. The long interval of misdiagnosis and the multiple, ineffective and potentially dangerous surgeries likely occurs for a variety of reasons, including: the rarity of the disease; a general lack of understanding of the disease; and difficulty in arriving at the diagnosis because symptoms are non-specific and overlap with other more prevalent functional bowel disorders (i.e., functional dyspepsia, idiopathic gastroparesis, IBS, chronic constipation). Long-term outcomes are poor despite medical and surgical therapies. In the study of 59 patients with CIP described above, four patients died of disease-related complications and 4 underwent small bowel transplantation (11). One-third of patients required long-term PN and two-thirds had nutritional deficiencies or limitations.

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Table 2
Symptoms and Signs of CIP

Common signs/symptoms
- Abdominal pain
- Abdominal distension
- Bloating
- Nausea/vomiting
- Constipation
- Diarrhea
  - Often due to bacterial overgrowth
- Weight loss
- Anorexia
- Nutritional deficiencies

Esophageal involvement
- Dysphagia
- Esophageal reflux/heartburn
- Atypical chest pain

Stomach
- Early satiety

Extra-intestinal
- Dysuria
- Abnormal bladder function
- Dilated ureter

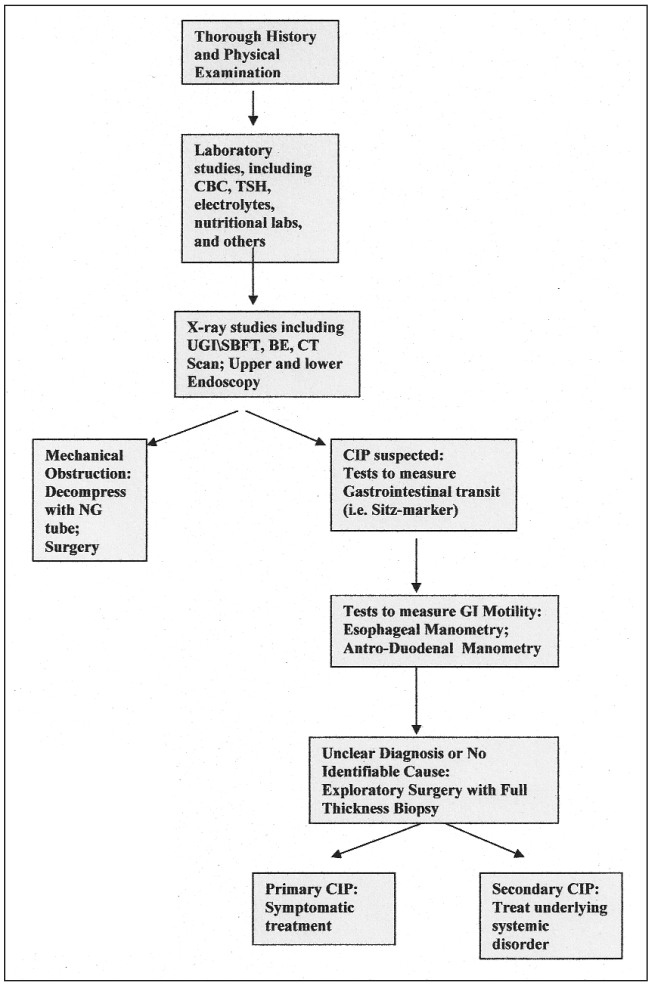

Figure 1. Algorithm: Diagnosis of CIP. CIP = Chronic intestinal pseudo-obstruction; UGI = Upper gastrointestinal series; SBFT = Small bowel follow-through; BE = Barium enema

Overall, only 11% of CIP patients are asymptomatic between subacute obstructive episodes and do not require chronic medical treatment. Approximately 20% of patients develop intractable abdominal pain and become opioid dependent (4).

MAKING THE DIAGNOSIS

Unfortunately, there is no specific biologic marker for CIP, therefore, a complete and thorough history and physical examination remains the cornerstone of making an accurate diagnosis. To diagnose CIP, patients should have symptoms for a minimum of six months (Table 2). A step-wise approach is used to make the diagnosis of CIP and generally includes pertinent laboratory studies, plain films of the abdomen, gastrointestinal transit measurements, and specialized tests of gastrointestinal motility (Figure 1).

To begin, patients are evaluated with a battery of laboratory tests including a complete blood count, erythrocyte sedimentation rate or C-reactive protein, serum electrolytes including calcium, magnesium and phosphorous, albumin, thyroid stimulating hormone, clotting time (which can be abnormal in patients who have bacterial overgrowth or severe nutritional problems), and specialized tests (i.e. ANA, AMA, anti-smooth muscle antibody, SPEP, anti-double stranded DNA, SCL-70 panel, anti-Hu) to eliminate the possibility of systemic diseases including autoimmune processes, malignancies, and endocrine disorders.

Next, patients should have an abdominal flat plate (KUB) to identify a possible site of obstruction. The diagnosis of CIP cannot be accurately made if there is no evidence of an obstruction on plain films. Plain films obtained during an acute attack typically reveal findings consistent with mechanical obstruction: distended bowel loops and air-fluid levels in the upright position. Computed tomography (CT) of the abdomen and pelvis is frequently performed due to symptoms of pain and concerns over possible mechanical obstruction. The CT scan may be able to identify bowel wall thickening or evidence of blockage or perforation. Barium studies to examine the upper gastrointestinal tract, followed by a barium enema (to assess the anatomy of the colon), are often required to rule out mechanical obstruction and provide evidence of

intestinal dilation secondary to pseudo-obstruction. Barium studies may also demonstrate a lack of peristalsis (seen in myopathic processes) or chaotic peristalsis (frequently seen in neuropathic processes). Alternatives to barium studies include water-soluble contrast or using small amounts of barium with air contrast. Endoscopic evaluation (upper endoscopy, colonoscopy, and capsule endoscopy) can detect masses, strictures, or physical obstruction, which in their absence, will help establish the diagnosis of CIP.

Next, tests to measure transit in the gastrointestinal tract are typically obtained. This is most commonly performed using a solid phase gastric emptying scan and a Sitz mark study (to measure colonic transit). Some specialized motility centers also perform transit studies of the small intestine using radioactive materials. Further support for the diagnosis of CIP, and clues to the possible underlying etiology, can often be obtained from intestinal manometry. Esophageal manometry will reveal abnormalities in esophageal motility in approximately 80% of patients with pseudo-obstruction. Studies with antroduodenal manometry (small bowel motility) may also reveal characteristic motility abnormalities. Esophageal manometry is performed at most hospitals, although antroduodenal manometry is typically performed only at specialized motility centers.

If the physician remains suspicious about the possibility of a mechanical obstruction, then exploratory laparotomy should be performed. At the same time, full thickness biopsies of the intestinal wall should also be obtained. These biopsies will show smooth muscle atrophy in the primary myopathic processes, neuropathic degeneration in the primary neuropathic disorders, and various findings for the secondary causes of CIP including fibrosis in primary systemic sclerosis, or evidence of amyloid or lymphoma (Table 3).

Table 3
Histological differences between myopathic and neuropathic CIP*

Myopathic
- Muscle degeneration
- Atrophy and fibrosis of one or both layers of the muscularis propria
- ± inflammatory cells

Neuropathic
- Dense infiltrate of lymphocytes and plasma cells surrounding myenteric plexus and axons
- Fragmentation and loss of axons
- Proliferation of glial cells
- ± inflammatory cells

*Some cases may have mixed myopathic and neuropathic histological findings

TREATMENT OPTIONS

Chronic intestinal pseudo-obstruction remains a challenge to treat. Therapy for secondary causes of CIP (i.e., scleroderma) should focus on treating the underlying disorder. This often includes correcting electrolyte abnormalities, managing dehydration, treating infections, using immunosuppressant agents for patients with collagen vascular diseases, initiating a gluten-free diet for pseudo-obstruction associated with celiac disease, or treating the underlying cancer that has caused a paraneoplastic syndrome.

Treatment for idiopathic or primary CIP, however, is often quite difficult (Table 4). The disease entity is rare and often goes unrecognized for long periods during which time patients are subjected to numerous treatments including repeated surgeries which have the potential for morbidity and mortality. In contrast to other gastrointestinal disorders, such as acid reflux disease or irritable bowel syndrome, CIP is extremely rare and therefore large, randomized controlled trials evaluating different treatment options are lacking, and treatment is based on clinical experience and the results of small studies or individual case reports. In a small, prospective study, only 1 of 20 patients with idiopathic CIP had symptomatic improvement with medication therapy (4).

Diet

In general, treatment should begin by correcting any nutritional deficiencies that may be present. In order to maximize oral intake, patients should be encouraged to take in small, frequent meals (five-six per day), with an emphasis on liquids and soft foods, while avoiding high fat solid foods and fiber. Foods high in fat content (>30% total calories) are thought to delay gastric emptying and cause postprandial fullness and nausea, while high fiber

Table 4
Treatment of Idiopathic or Primary CIP

Erythromycin, a macrolide antibiotic that acts as an agonist to the motilin receptor, can be given either orally or intravenously. Doses in the range of 50–200 mg orally, or 50–100 mg intravenously (iv), approximately 30 minutes before meals, have been shown to be effective in accelerating gastric emptying and improving symptoms of CIP (16).

Cisapride, a mixed 5HT-4 receptor agonist/5HT-3 receptor antagonist, is not available for routine clinical use, although it can be obtained in very limited circumstances. Cisapride was removed from the market in July 2000 because of drug interactions leading to an increased risk of cardiac arrhythmias.

Metoclopramide, a commonly used anti-emetic, is a dopamine antagonist that exerts its prokinetic effects by increasing acetylcholine release. Metoclopramide is commonly given as 10–20 mg orally or IV 30 minutes before meals and at bedtime. Mild adverse reactions include fatigue, somnolence, anxiety, jitteriness, or depression may occur. More severe adverse events including extrapyramidal side effects (i.e., tardive dyskinesia) are fortunately, uncommon.

Domperidone is similar to metoclopramide in that it acts as an antagonist at dopamine receptors. Domperidone does not readily cross the blood-brain-barrier, and therefore, does not have the potential for the central nervous system side affects that metoclopramide have. Doses range between 10–20 mg orally 30 minutes before meals and at bedtime. Domperidone is not FDA approved for use in the United States.

Octreotide, a long acting somatostatin analogue, stimulates small intestine motility when given in low doses. It is most effective in patients who have a neuropathic process as the underlying etiology of their CIP, since it requires the presence of smooth muscle in order to be effective. It is usually given in doses of 25–50 µg subcutaneously after both the morning and evening meals.

Tegaserod, a specific 5-HT4 receptor agonist, improves gastric emptying, colonic transit, and orocecal transit time, and was approved for use only in women with irritable bowel syndrome and constipation (17). Unfortunately, tegaserod is now available only for life-threatening emergencies due to concerns that it may increase the risk of cardiovascular complications (18).

Lubiprostone, a chloride channel activator approved for the treatment of chronic constipation and women with IBS and constipation, has not been studied in CIP patients (19).

products are associated with abdominal bloating, bezoar formation, and abdominal discomfort. Lactose often needs to be avoided because of the high incidence of lactose intolerance in the general population (25%) and the potential to worsen abdominal bloating and discomfort. Poorly absorbed sugar alcohols may also aggravate symptoms (12). Numerous nutritional supplements are currently available and are especially useful in malnourished patients. A daily multivitamin should be taken, and patients should receive supplemental essential vitamins, minerals, and electrolytes as needed. Of note, bacterial overgrowth and chronic diarrhea may lead to malabsorption of fat soluble vitamins (A, D, E, and K) and B12 deficiency. Referral to a registered dietitian can be very helpful for many patients for nutritional education and the development of a patient specific diet.

Nutrition Support

Enteral Feeding. If dietary changes are unsuccessful resulting in unmet nutritional requirements and continued weight loss, then enteral nutrition support is the next step. In a retrospective study, Scolapio and colleagues demonstrated that patients with CIP can generally be managed with EN using a standard formula (13). A trial of nasogastric or nasojejunal feeding should be tried prior to placement of a more permanent percutaneous feeding tube. If patients are able to tolerate fiber-free EN with few symptoms and regular bowel movements (it is important for the clinician to find out the normal stool habits of the individual patient), then consideration can be given for placement of a percutaneous gastrostomy or gastro-jejunostomy tube, or direct placement of a jejunostomy tube, to bypass a dysfunctional stomach. If delayed gastric emptying is present, then direct feeding of the small intestine is preferred, unless the patient would benefit from having a gastric venting port. Continuous or cycled EN (10–12 hours overnight) is often better tolerated than bolus feedings. A trial of elemental feeding prior to PN is warranted.

Parenteral Feeding. Ideally, PN should be avoided due to the risks of cellulitis, sepsis, thrombus formation, and catheter migration or displacement. However, a large proportion of CIP patients will eventually require parenteral nourishment.

Table 5
Medications Commonly Used to Treat Nausea in CIP

Antihistamines
- Dimenhydrinate (Dramamine)
- Promethazine (Phenergan)
- Meclizine (Antivert)
- Cyclizine (Marezine)
- Diphenhydramine (Benadryl)

Anticholinergics
- Scopolamine

Phenothiazines
- Prochlorperazine (Compazine)
- Chlorpromazine (Thorazine)
- Promethazine (Phenergan)

Butyrophenones
- Haloperidol (Haldol)
- Droperidol (Inapsine)

Dopaminergic Antagonists
- Metoclopramide (Reglan)
- Domperidone (Motilium)

Serotonin Receptor Antagonists
- Ondansetron (Zofran)
- Granisetron (Kytril)
- Dolasetron (Anzemet)

Miscellaneous
- Lorazepam (Ativan)
- Prednisone
- Dexamethasone
- Dronabinol (Marinol)
- Trimethobenzamide (Tigan)
- Ginger

Decompression Measures

Decompression of distended intestinal segments via intermittent nasogastric suction, rectal tubes, or endoscopy is helpful for many patients. Given a lack of clinical studies addressing this issue, there are no firm guidelines on when such intervention should be undertaken. Decompression of the distended intestinal segment may include a "venting" enterostomy. These are typically placed in the stomach, although some patients with feeding J-tubes also use them for venting purposes. As described by Pitt and colleagues, patients with surgically placed gastrostomy tubes had a lower rate of hospital admissions (0.2 vs 1.2 admissions per patient-year) (14), and in another study, admissions decreased by 0.5 to 1.0 (15).

Prokinetic Agents

Regardless of whether the underlying process is myopathic or neuropathic in nature, all patients with CIP have disordered gastrointestinal tract motility. Multiple prokinetic agents have been used in an attempt to promote normal intestinal motility; however, there are few investigational studies available to demonstrate the efficacy of any of these agents in CIP (Table 4).

Antibiotics

Intestinal stasis may lead to small intestine bacterial overgrowth and diarrhea, with resultant malabsorption, weight loss and the development of multiple vitamin deficiencies. Rotating antibiotics may relieve symptoms of diarrhea and bloating and improve the nutritional status in many patients with CIP. No controlled trials have been performed to determine which antibiotics are best, however many clinicians have patients use a different antibiotic every month for seven-to-10 days over a five-to-six month cycle. (Please see the following review for more information about small bowel bacterial overgrowth: DiBaise JK. Small Intestinal Bacterial Overgrowth: Nutritional Consequences and Patients at Risk. *Practical Gastroenterology,* 2008;32(12):15).

Antiemetics

Patients with CIP may suffer from recurrent bouts of nausea and vomiting during an episode of pseudo-obstruction, or they may have nausea on a near daily basis. There is no single agent particularly suited for the treatment of nausea and vomiting in CIP. Rather, each patient needs to be assessed individually to determine current medication use, previous trials of antiemetics, adverse reactions, and financial status. Classes of medications commonly used to treat nausea are shown in Table 5.

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Small Bowel Transplantation

For patients with intestinal failure and life-threatening PN-related complications, small bowel transplantation has become an accepted therapy, although data remains limited. Of four patients who underwent small bowel transplantation for primary CIP, three were alive at 24 months and two had improvement in digestive symptoms after resuming an oral diet, however, all remained on at least partial parenteral supplementation (11). Intestinal transplantation is only available at a small number of specialized centers in the United States.

CONCLUSION

CIP is a rare, disabling, and potentially life-threatening neuromuscular disorder of the digestive tract simulating mechanical obstruction in the absence of an anatomical lesion. As demonstrated by the two cases provided above, it often goes unrecognized and misdiagnosed for long periods of time given its nonspecific symptoms, clinical overlap with more common conditions, and the absence of a biological marker of disease. Maintaining a high index of suspicion together with a careful history and physical examination can guide appropriate further diagnostic testing to arrive at the correct diagnosis. Unfortunately, except for cases in which a secondary cause can be identified, management is largely supportive. Ensuring appropriate nutrition and managing complications from CIP or its associated treatments is paramount. ■

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