

CHRONIC INTESTINAL PSEUDO-OBSTRUCTION

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(1-18-08)

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I. INTRODUCTION

Chronic intestinal pseudo-obstruction (CIP) is a disorder of the gastrointestinal tract characterized by symptoms and signs which suggest mechanical obstruction of the intestinal tract, although no obstruction is present. While the clinical symptoms and signs of CIP are usually indistinguishable from mechanical obstruction of the intestinal tract (which can develop due to scar tissue, adhesions, or malignancy), the etiology (the underlying cause), the underlying pathophysiology, and the treatment are quite different. This review will focus on the following aspects of CIP: understanding the impact of pseudo-obstruction; describing the causes and mechanisms of CIP; common symptoms and signs; diagnosing CIP; and finally, treatment options.

II. 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 were found to have normal findings at the time of exploratory surgery.¹ The exact prevalence (the number of people with a disease at a specific point in time) of CIP remains unknown, although it is estimated that approximately 100 infants are born each year in the United States with congenital pseudo-obstruction.² This number, however, significantly underestimates the total number of new cases each year, as it does not include the large number of adult patients who develop 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 showed that a large number of CIP patients require central venous access (i.e., Mediport) or a percutaneous gastrostomy tube (i.e., G-tube) in order to provide 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 the one published report to date, Mann and colleagues described CIP patients as frequently being dependent upon supplemental intravenous or enteral nutrition, using multiple expensive medications (often without success), and often becoming dependent on narcotics due to chronic abdominal pain.⁴

III. IDENTIFYING THE CAUSE AND MECHANISM OF DISEASE

Chronic intestinal pseudo-obstruction is generally grouped into 3 categories: primary (either neuropathic or myopathic in nature); secondary (due to collagen vascular diseases, endocrine disorders, malignancies, neurologic disorders, etc.); or idiopathic (cause unknown). Table 1 reviews this classification system and also lists conditions commonly associated with CIP.

The unifying characteristic of CIP is that of disordered gastrointestinal tract motility. In primary CIP, this may stem from an inherent (intrinsic) defect in the normal mechanisms that control gastrointestinal tract motility, for example, either injury to the muscle (a myopathy) or to the nervous system (a neuropathy). Injury to the nervous system in patients with CIP typically involves injury to the enteric nervous system, although injury may also occur in the autonomic nervous system (the sympathetic and parasympathetic nerves). In addition, within each major group (neuropathic or myopathic) CIP can also be categorized into 1 of 3 subcategories: congenital (present since birth); familial (presumably genetic in nature); or sporadic. These subcategories may then be further classified to represent areas of intestinal involvement (i.e., colon or small intestine or stomach or esophagus or a combination of all 4) and potential causes (see the middle column of Table 1). Thus, any primary CIP patient with a family history of pseudo-obstruction would be considered to have either primary myopathic or neuropathic familial intestinal pseudo-obstruction. In contrast, those patients without an identifiable family history of pseudo-obstruction would be classified as having sporadic CIP, which would be either myopathic or neuropathic in nature.

Secondary causes of CIP include collagen vascular disorders, endocrine disorders, neurologic disorders, medications and miscellaneous other disorders (see 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.⁵ Viruses have also been implicated as a possible causative factor in CIP.⁶

IV. CLINICAL PRESENTATION (SYMPTOMS AND SIGNS)

An analysis by Mann and colleagues found that the median age of symptom onset was 17 years with a range of 2 weeks to 59 years.⁴ The frequency and severity of symptoms varies remarkably from patient to patient depending upon the location and the extent of the gastrointestinal tract involved. The most common symptoms include pain (80%), nausea and vomiting (75%), constipation (40%), and diarrhea (20%).⁷

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

Patients may have symptoms of early satiety (filling up quickly after eating a meal) and upper abdominal fullness if the stomach is involved. Bloating and abdominal distention are frequently seen and patients may complain about “looking pregnant” or having to loosen their clothes in order to allow them to fit properly.

Many patients with CIP have symptoms of chronic constipation (i.e., infrequent stools, straining, and incomplete evacuation). Diarrhea can also occur in patients with CIP and is likely secondary to intestinal stasis (slow movement of materials through the intestinal tract) which promotes bacterial overgrowth. Patients with CIP may suffer from malabsorption and develop nutritional

deficiencies secondary to bacterial overgrowth. Weight loss and anorexia (loss of appetite) is common in many patients with intestinal pseudo-obstruction

Patients with CIP typically suffer from abdominal pain. For some patients, the pain is intermittent in nature, and occurs only during an acute episode or crisis. For other patients, however, the pain is chronic in nature. The pain can be located anywhere in the abdomen, depending upon the location (i.e., stomach or colon or small intestine) and the extent (i.e., the entire colon vs. a small segment of the small intestine) of bowel that is involved. Many patients characterize the pain as sharp, stabbing, or twisting, although others describe it as more of a pressure, ache, or discomfort. Pain typically worsens as bloating and abdominal distension progresses and improves as the crisis resolves.

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

V. MAKING THE DIAGNOSIS

A complete and thorough history and physical examination remains the cornerstone of making the diagnosis of CIP. Warning signs, which include unintentional weight loss (more than 5% of ideal body weight), hematemesis (vomiting blood), hematochezia (bright red blood from the rectum), or signs of complete obstruction, warrant a more urgent work-up and possible early surgical intervention. Since it may be difficult to distinguish the patient with CIP from the

patient with mechanical obstruction, it is important to review the history (previous surgeries, the presence of adhesions, diverticuli, and a history of intestinal cancer in the patient or in family members), and perform a thorough physical examination. Patients should be carefully questioned about current and past medication use, a family history of similar disorders, and any prior diagnostic tests performed in the evaluation of these symptoms.

To diagnose CIP, patients should have symptoms for a minimum of 6 months. A step-wise approach is used to make the diagnosis of CIP and generally includes laboratory studies, x-ray studies, test to measure gastrointestinal transit, and if necessary, specialized tests of gastrointestinal motility.

To begin, patients are evaluated with a battery of laboratory tests including a complete blood count (to check for anemia or an infection), serum electrolytes, albumin (a measure of nutritional status), thyroid hormone, clotting time (which can be abnormal in patients who have bacterial overgrowth or severe nutritional problems), and specialized tests to eliminate the possibility of systemic diseases including autoimmune processes, malignancies, and endocrine disorders (see Figure 1).

Next, patients should have a plain x-ray of the abdomen (an abdominal flat plate or KUB) to identify a possible site of obstruction. The diagnosis of CIP cannot be accurately made there is no evidence of an obstruction on an abdominal x-ray. Computed tomography (abdominal CT scan) 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 a blockage or a

perforation. Barium studies (upper gastrointestinal series with small bowel follow-through) 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 (seen in neuropathic processes). Of note, patients should always be cautioned that there is a small risk of barium impaction if complete obstruction of the bowel is present and barium is used. Alternatives to barium studies include water-soluble contrast or using small amounts of barium with air contrast. Endoscopic evaluation (upper endoscopy, colonoscopy, capsule endoscopy) can detect masses, strictures, or physical obstruction, which in their absence, will help establish the diagnosis of CIP.

Next, patients generally undergo tests to measure transit in the gastrointestinal tract. This is most commonly performed using a solid phase gastric emptying scan (to measure emptying of the stomach) and a Sitz marker 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 surgery (laparotomy) should be performed. At the same time, full thickness biopsies of the intestinal wall should also be performed. These biopsies will show smooth muscle atrophy (wasting) 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.

VI. 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 electrolytes, 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.

Treating idiopathic or primary CIP, however, is often quite difficult. Many patients and physicians are tempted to find a “quick fix” which may include ill-planned or repeated surgeries, radical treatments, and injudicious use of narcotics. All of these have the potential to make the patient much worse. In contrast to other gastrointestinal disorders, such as acid reflux disease or irritable

bowel syndrome, 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.

A. Diet

In general, treatment should begin by correcting any nutritional deficiencies that may be present. As always, oral nutrition is preferred. In order to maximize enteral intake patients should be encouraged to take in small, frequent meals (5-6 per day), with an emphasis on liquids and soft foods, while avoiding fats and fiber. Foods high in fat content (>30% total calories) delay gastric emptying and may cause postprandial fullness, while high fiber and high residue 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. Numerous nutritional supplements are currently available (i.e., Enlive) and are especially useful in malnourished patients. These supplements are all high in calories and low in residue; the fat concentration varies between each supplement. 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. If these dietary changes are not successful, then alternatives include using elemental feedings (e.g., Peptamen) and the use of dietary supplements with medium-chain triglycerides. Referral to a registered dietitian can be very helpful

for many patients for nutritional education and the development of a patient specific diet.

B. Tube Feedings and TPN

If nutritional requirements are not met by oral intake and patients continue to lose weight enteral access with tube feedings is the next step. A retrospective study by Scolapio and colleagues demonstrated that patients with CIP can generally be successfully managed with tube feeds using a standard nonelemental formula.⁹ A trial of nasogastric or nasoenteric tube feedings should be tried prior to placement of percutaneous feeding tubes (e.g., G-tubes). If patients are able to tolerate tube feedings with low residuals, few symptoms, and regular bowel movements, then consideration should be given for placement of a percutaneous gastrostomy, G-J tube (gastro-jejunostomy), or direct placement of a jejunostomy tube, to bypass the dysfunctional stomach. If delayed gastric emptying is present, then direct feeding of the small intestine is preferred. Continuous feeding or cyclical feeding (12 hours of continuous feeding during the night) usually is better tolerated than large bolus feedings.

Ideally, parenteral nutrition should be avoided due to the risks of cellulitis, sepsis, blood clot formation, and catheter migration or displacement. However, a large proportion of CIP patients will eventually require parenteral nourishment at some point. Patients should receive approximately 25 kcal/kg/day and lipids should supply approximately 30% of total parenteral calories with 1.0-1.5 g/kg/day protein and dextrose providing the remainder of required calories.¹⁰

C. Decompression Measures

Ideally, the best therapy for CIP would be to treat the underlying process (i.e., the underlying neuropathy or myopathy). Unfortunately, that is not an option at present. Decompression of distended intestinal segments via intermittent nasogastric suction, rectal tubes, or endoscopy is helpful for many patients. A lack of clinical studies addressing this issue means that 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 admissions per patient-year) after the procedure than prior to the procedure (1.2 admissions per patient-year).¹¹

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.

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 the symptoms of CIP.¹²

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 effects that metoclopramide does. 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 ug 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.¹³ Unfortunately, tegaserod is not currently available due to concerns that it may increase the risk of cardiovascular complications.¹⁴

E. 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 7-10 days over a 5-6 month cycle.

F. 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 3.

VII. REFERENCES

1. Dudley HAF, Sinclair ISR, McLaren IF, et al. Intestinal pseudo-obstruction. *J R Coll Surg Edin* 1958;3:206-217.
2. Di Lorenzo C. Pseudo-obstruction: Current Approaches. *Gastroenterology* 1999;116:980-987.
3. Schwankovsky L, Mousa H, Rowhani A, et al. Quality of life outcomes in congenital chronic intestinal pseudo-obstruction. *Dig Dis Sci* 2002;47:1965-1968.
4. Mann SD, Debinski HS, Kamm MA. Clinical characteristics of chronic idiopathic intestinal pseudo-obstruction in adults. *Gut* 1997;41:675-681.
5. Krishnamurthy S, Schuffler MD. Pathology of neuromuscular disorders of the small intestine and colon. *Gastroenterology* 1987;93:610-639.
6. Debinski HS, Kamm MA, Talbot IC, et al. DNA viruses in the pathogenesis of sporadic chronic idiopathic intestinal pseudo-obstruction. *Gut* 1997;41:100-106.
7. Stanghellini V, Camilleri M, Malagelada JR. Chronic idiopathic intestinal pseudo-obstruction: clinical and intestinal manometric findings. *Gut* 1987;28:5-12.
8. Sullivan MA, Snape WJ, Matarazzo SA, et al. Gastrointestinal myoelectrical activity in idiopathic intestinal pseudo-obstruction. *New Eng J Med* 1977;297:233-238.
9. Scolapio JS, Camilleri M, Romano M. Audit of the treatment of malnutrition due to chronic intestinal pseudo-obstruction with enteral nutrition. *Nutr Clin Prac* 1999;14:29-32.
10. Scolapio JS, Ukleja A, Bouras EP, Romano M. Nutritional management of chronic intestinal pseudo-obstruction. *J Clin Gastroenterology* 1999;28:306-312.
11. Pitt HA, Mann LL, Berquist WE, et al. Chronic intestinal pseudo-obstruction: Management with total parenteral nutrition and a venting enterostomy. *Arch Surg* 1985;120:614-618.

12. Minami T, Nishibayashi H, Shinomura Y, Matsuzawa Y. Effects of erythromycin in chronic idiopathic intestinal pseudo-obstruction. *J Gastroenterology* 1996;31:855-859.
13. Lacy BE and Yu S. Tegaserod: A new 5-HT₄ agonist. *J Clin Gastroenterology* 2002;34:27-33.
14. <http://www.fda.gov/cder/drug/advisory/tegaserod.htm>. Accessed 1-14-08.

Table 1. CLASSIFICATION OF CHRONIC INTESTINAL PSEUDO-OBSTRUCTION

PRIMARY	SECONDARY	IDIOPATHIC
I. Myopathic	Collagen Vascular Diseases	
A. Congenital	Primary Systemic Sclerosis	
B. Familial	Systemic Lupus Erythematosus	
C. Sporadic	Dermatomyositis/Polymyositis	
	Periarteritis nodosa	
	Mixed connective tissue disorders	
	Rheumatoid arthritis	
	Endocrine Disorders	
	Hypothyroidism\parathyroid	
	Diabetes mellitus	
II. Neuropathic	Neurologic disorders	
A. Congenital	Parkinson's disease	
B. Familial	Hirschsprung's disease	
C. Sporadic	Chagas' disease	
	Intestinal hypoganglionosis	
	Drug Associated	
	Tricyclic antidepressants	
	Anticholinergic agents	
	Ganglionic blockers	
	AntiParkinsonian drugs	
	Phenothiazines	
	Clonidine	
	Miscellaneous*	

*Miscellaneous processes may include: Celiac disease, infiltrative diseases (amyloid, lymphoma), neoplastic, familial dysautonomia, metabolic (low potassium, magnesium, phosphorous), jejunoleal bypass, mesenteric vascular insufficiency, alcoholism, viral infections, radiation, and after organ transplant.

Table 2. Treatment for CIP.

Diet	Low Residue, Low Fiber, Low Fat, Low Osmolality
Nutrition	Ensure adequate Calories (25 kcal/kg/day) Ensure adequate Vitamins, Minerals, and Electrolytes
• Must Have Appropriate Access	PEG, G-J Tube, Jejunostomy Tube, Central Access
Start Supplemental Feeding, Tube Feeding or Parenteral Feeding based on Adequacy of Oral Intake	
Decompression	Nasogastric or Nasoenteric Decompression, Rectal Tube Endoscopic Decompression, “Venting” Enterostomy, Cecostomy tube placement
Prokinetics	Erythromycin Cisapride (investigational use) Metoclopramide Domperidone (Not FDA approved) Tegaserod (not currently available) Octreotide
Antibiotics	Amoxicillin - Clavulanate Fluroquinolones Cephalosporins and Metronidazole Tetracycline Maintenance Therapy for Recurrent Bacterial Overgrowth
Surgery	Intestinal Resection

Table 3. MEDICATIONS COMMONLY USED TO TREAT NAUSEA

- **ANTI-HISTAMINES**
 - 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
- Marinol (Dronabinol)
- Ginger

Figure 1.

Algorithm: Diagnosis of CIP

