

Cystic Fibrosis

Care Guidelines for CF-Related Abdominal Pain

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This document is based on a consensus of evidence and/or clinical expert opinion.

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General Age Range Guide

| Infant | Preschool | Child | Adolescent | Adult |
|--------------|--------------|---------------|----------------|------------|
| 0 to 2 years | 2 to 6 years | 6 to 12 years | 12 to 18 years | ≥ 18 years |

Abbreviation Guide

CF Cystic Fibrosis

CFTR Cystic Fibrosis Transmembrane Regulator

CT Computerized Tomography

DIOS Distal Intestinal Obstructive Syndrome

PERT Pancreatic Enzyme Replacement Therapy

Introduction

Abdominal pain is a common symptom in patients with cystic fibrosis (CF) and there are a number of gastro-intestinal complications of CF which must be considered. It should also be remembered that other typical causes of abdominal pain in the general population can also affect patients with CF. Causes could include acute pancreatitis, gallstones (choledocholithiasis), or even simple bloating. A comprehensive review of all the possible causes of abdominal pain is beyond the scope of this care guideline. Instead, we focus on the recognitions and management of distal intestinal obstruction syndrome, and the broader differential diagnosis in a CF patient presenting with abdominal pain.

Distal Intestinal Obstruction Syndrome

Distal Intestinal Obstructive Syndrome (DIOS) is a complication unique to the CF population and occurs in 10-24% of patients with CF^{1,2} with a higher incidence in those with pancreatic insufficiency.

Definition

The presentation of DIOS is variable representing the spectrum of incomplete to complete intestinal obstruction.²

- **Complete DIOS:** radiological and clinical evidence of complete obstruction associated with abdominal distension and a palpable ileocecal mass in the right iliac fossa
- **Incomplete DIOS:** colicky abdominal pain or distension coupled with a palpable ileocecal mass in the right iliac fossa (more so in children) but without evidence of complete intestinal obstruction

Pathophysiology

- DIOS is characterised by small intestinal blockage by a plug of muco-feculent material, most commonly occurring at the junction of the ileum and the proximal ascending colon in the right iliac fossa.
- The pathophysiology is complex and not fully understood. It is proposed that CFTR dysfunction in the intestinal lumen leads to increased water and sodium absorption causing increased mucus viscosity in the stool.
- Multiple risk factors have been identified for the development of DIOS:³
 - history of meconium ileus
 - female gender⁴
 - dehydration

- severe CFTR genotype (e.g. homozygous deltaF508 mutations)
- pancreatic insufficiency
- history of abdominal surgery/adhesions
- poorly controlled fat malabsorption/poor PERT compliance
- post organ transplantation
- use of narcotic analgesics

Clinical Features

- A history of constipation or less frequent bowel movements may be present but recent bowel opening does not exclude DIOS. In some cases, patients can present with diarrhea representing overflow past the obstructive mass.
- Patients present with crampy, colicky abdominal pain resulting from recurrent partial or complete intestinal obstruction. Pain might be generalised and intermittent but as muco-feculent material progressively obstructs the bowel, features of obstruction evolve with acute periumbilical or right lower quadrant pain, vomiting, and abdominal distension.

Screening / Investigations

a. Imaging

- Plain abdominal x-ray is the key initial investigation, with typical findings of generalised small bowel dilatation with bubbly faecal mass in the right iliac fossa (without large bowel involvement).
- CT scan of the abdomen can help in further diagnosis of stricture, adhesions in patients with previous abdominal surgeries, and intussusception (and might provide an alternate non-obstructive diagnosis).
- Abdominal ultrasound can also be used to detail abdominal anatomy, free fluid, bowel thickening, appendix mass, intussusception, gallstones, and evidence for portal hypertension.
- Barium/hypaque sodium enema performed by specialist radiologist can diagnose DIOS with the potential for therapeutic benefits.

b. Other investigations

- Obtain a urinalysis to exclude urinary tract infection
- Obtain blood work – CBC, BUN, Creatinine, electrolytes, Liver function tests, Albumin, Amylase/Lipase, CRP, Calcium, Magnesium, and Phosphate.

Management Recommendations

1. First line therapy should be to medically manage.

Rationale:

- Several retrospective studies have demonstrated resolution of DIOS in 70 to 80% of cases with medical management.^{5, 6}
2. For incomplete DIOS (and no signs of peritoneal involvement or vomiting), use a stepwise washout approach.

| Stepwise Washout Approach | |
|---------------------------|---|
| a | Ensure pancreatic enzyme dose is properly titrated to dietary fat intake. |
| b | Ensure proper hydration. Administer intravenously if necessary |
| c | Administer laxatives orally (PO) - see Laxative Options |
| d | If PO laxatives fail, consider oral or colonic lavage - see Treatment for Complete DIOS |

3. For complete DIOS presenting with features of acute obstruction (persistent vomiting or bilious vomiting, abdominal distention, or failed washout therapy):
 - Focus management on gastric decompression, rehydration, colonic lavage, and surgical or gastrointestinal referral.
 - Obtain baseline blood work: CBC, BUN, Creatinine, electrolytes (including Calcium, Magnesium, Phosphate), Liver function tests, Albumin, Amylase/Lipase, CRP, Arterial Blood Gases.
 - Avoid treating pain with opiate analgesics

| Treatment for Complete DIOS | |
|-----------------------------|--|
| a) Gastric Decompression | <ul style="list-style-type: none"> ■ Nothing by mouth (NPO) ■ Nasogastric (NG) tube on free drainage |
| b) Rehydration | <ul style="list-style-type: none"> ■ Intravenous fluids <ul style="list-style-type: none"> ■ Maintenance of 0.9%NaCl + 5% Dextrose ■ Replacement of 50% of NG losses |

| Treatment for Complete DIOS | |
|---|---|
| c) Colonic lavage (orally or rectally) | <ul style="list-style-type: none"> ■ If not vomiting, consider a trial of PO/NG GoLytely ■ N-acetylcysteine (Mucomyst) enema (PR) ■ Omnipaque (pediatrics) Gastrograffin enema (adults) PR under radiological guidance only. <ul style="list-style-type: none"> ■ Watch for dehydration. ■ Perform a plain abdominal x-ray at 1 hour to exclude massive dilation. ■ If massive dilation is present, make urgent referral to surgeon. |
| d) Referral* for general surgery or gastroenterology review | <ul style="list-style-type: none"> ■ If condition deteriorating or there is a failed response to conservative management |

*Successful cases of colonoscopy have been reported⁷ and might help avoid a laparotomy.

Laxative Options for DIOS episodes

| Laxative | Dose | Mild | Moderate | Severe | Severe w/ complete obstr |
|---------------------------|---|------|----------|--------|--------------------------|
| Docusate/Senna | Preschool: ½ to 1 tablet PO OD | X | | | |
| | Children: 1 to 2 tablets PO OD | X | | | |
| | Adolescent + Adults: 2 tablets PO OD | X | | | |
| Polyethalene Glycol (PEG) | PEG 3350 <ul style="list-style-type: none"> ■ 2g/kg/day, up to maximum of 80 to 100g/day | | X | X | |
| | PEG 3350 with Electrolytes (ready to use iso-osmotic solution) <ul style="list-style-type: none"> ■ 20 to 40mL/kg/hour, up to maximum of 1 Litre/hour over 8 hours ■ Can be given PO, or by NG or Gastrostomy | | X | X | |
| Lactulose | Give PO | | | | |
| | Preschool + Children: <ul style="list-style-type: none"> ■ 1 to 3mL/kg/day, divided doses BID, up to maximum of 60mL/day | | X | | |
| | Adolescent + Adults: <ul style="list-style-type: none"> ■ 20 to 30mL BID to QID | | X | X | |

| Laxative | Dose | Mild | Moderate | Severe | Severe w/ complete obstr |
|--------------------------|---|------|----------|--------|-----------------------------|
| Golytely® | Give PO or by NG Give until rectal fluid is clear | | | | |
| | Preschool + Children: ■ 25mg/kg/hour | | X | X | |
| Gastrograffin | Adolescent + Adults: ■ Titrate to patient's size ■ Can be up to 1 Litre/hour until rectal effluent is clear (maximum of 8L over 8 hours) | | X | X | |
| | Oral intestinal lavage PO or NG Can be given per rectum (PR) | | | | |
| | Adolescent + Adults: ■ 100mL mixed in 400mL of fruit juice or water PO/ NG OD ■ 100mL mixed in 400mL of water PR ■ For complete obstruction (vomiting), administer under fluoroscopic guidance to visually confirm clearance of the obstruction | | X | X | |
| Omnipaque | Give PR by radiologist under fluoroscopic guidance | | | | |
| | Infant, Preschool + Children: ■ 100mL mixed in 100mL of water | | | X | X |
| Phosphate enema (Fleet®) | May repeat once | | | | |
| | Preschool + Children: ■ 65mL PR X 1 | | X | | |
| | Adolescent + Adults: ■ 130mL PR X 1 ■ With 30mL of 20% N-acetylcysteine solution | | X | | |
| | | | | X | |

| Laxative | Dose | Mild | Moderate | Severe | Severe w/ complete obstr |
|-----------------------------------|---|------|----------|--------|-----------------------------|
| N-acetylcysteine enema (Mucomyst) | Dilute with normal saline to desired concentration | | | | |
| | Preschool + Children: <ul style="list-style-type: none"> ■ Begin with 100mL of 4 to 6% solution PR Higher concentrations (10 to 20%) appear to increase fluid in the bowel and could lead to more adverse effects ■ Give BID to QID | | X | | |
| | Adolescent + Adults: <ul style="list-style-type: none"> ■ 100mL of 10% solution PR (with 20% solution, dilute with equal amount of normal saline) ■ Give OD to QID | | X | | X |
| | <ul style="list-style-type: none"> ■ Can be given PO/NG* 10 to 30 mL of 10% solution mixed in 120mL fruit juice or soda TID to QID *Expensive, poorly tolerated, can take 2 to 3 days before effects are seen | | | X | |

Prevention of DIOS

- Ensure up to date assessment by a CF dietitian.
Check compliance with:
 - enzyme supplements
 - dose
 - timing of intake (always with snacks)
 - how they are taken - open or swallowed whole
- An extra dose at the end of a meal might help in those with delayed gastric emptying.
- Check storage of pancreatic enzymes. They are made inactive by heat, for example in a car glove box in the summer.
- Ensure adequate dietary fibre.
- For children, consider toilet routine with positive reinforcement star charts for children, or consider psychology input.
- Consider prescribing laxatives:

- Lactulose: 7.5 to 10mL, PO, OD
- PEG 3350
- Consider doing an estimation of stool fat (by doing a 3 day collection or semi-quantitative stool fat stain).
- Check for undiagnosed liver disease by Liver function testing and/or ultrasound abdomen. Consider ursodeoxycholic acid (might improve the fat absorption).
- Exclude celiac disease with blood test for tissue transglutaminase (tTG) antibodies.
- Consider optimising the efficacy of the pancreatic enzymes with addition of:
 - Ranitidine: 2 to 4mg/kg/day, PO, divided twice daily (Q12H)
 - Omeprazole (Losec): 0.7 to 3.5mg/kg/day, PO, OD, up to a maximum of 3.5 mg/kg/day or 80mg/day.
 - Domperidone: 1.2 to 2.4 mg/kg/24 hr, divided TID to QID.

Other Causes of Abdominal Pain in CF

Other causes of abdominal pain in CF can present similarly to DIOS with severe abdominal pain and a palpable mass including simple constipation, volvulus, intussusception, appendicitis, and fibrosing colonopathy. It is important to make an accurate diagnosis, as several of the other pathologies would require prompt surgical intervention whilst DIOS can usually be successfully managed medically.

Intussusception

- Can present with features similar to DIOS with abdominal pain and a palpable mass.
- It is more common in CF patients than the general population, likely due to the increased viscosity of the bowel contents causing an inflammatory lead-point.
- In a series of CF patients with intussusception⁸, the mean age for diagnosis was 9.8 years, much older than the typical presentation of idiopathic intussusception in the general population (which occurs most commonly under the age of two years).
- CT scan or ultrasound can help make the diagnosis.
- Management with enema reduction under fluoroscopic guidance is usually successful.

Appendicitis

- Diagnosing appendicitis can be challenging and difficult to differentiate from DIOS in CF patients, as both conditions typically present with right iliac fossa pain and tenderness.
- The incidence of appendicitis has been found to be lower than the general population (1.5% in CF, 7% in general population)⁹. This is possibly due to a relative protection of the appendix by inspissated mucus.
- Appendicitis in CF patients is associated with a higher complication rate such as perforation and abscess formation.
- Radiologically, appendicitis is more difficult to diagnose due to the mucous distension of the appendix in patients with CF.¹⁰

Volvulus

- Volvulus is uncommon surgical condition in the general population. While it has been reported in CF, it is not known if incidence is higher or lower in the CF population.
- Presentation is typical for bowel obstruction with abdominal pain, vomiting, and abdominal distension.
- Diagnosis is with imaging using plain X-ray, CT scan, or barium enema.

Fibrosing colonopathy

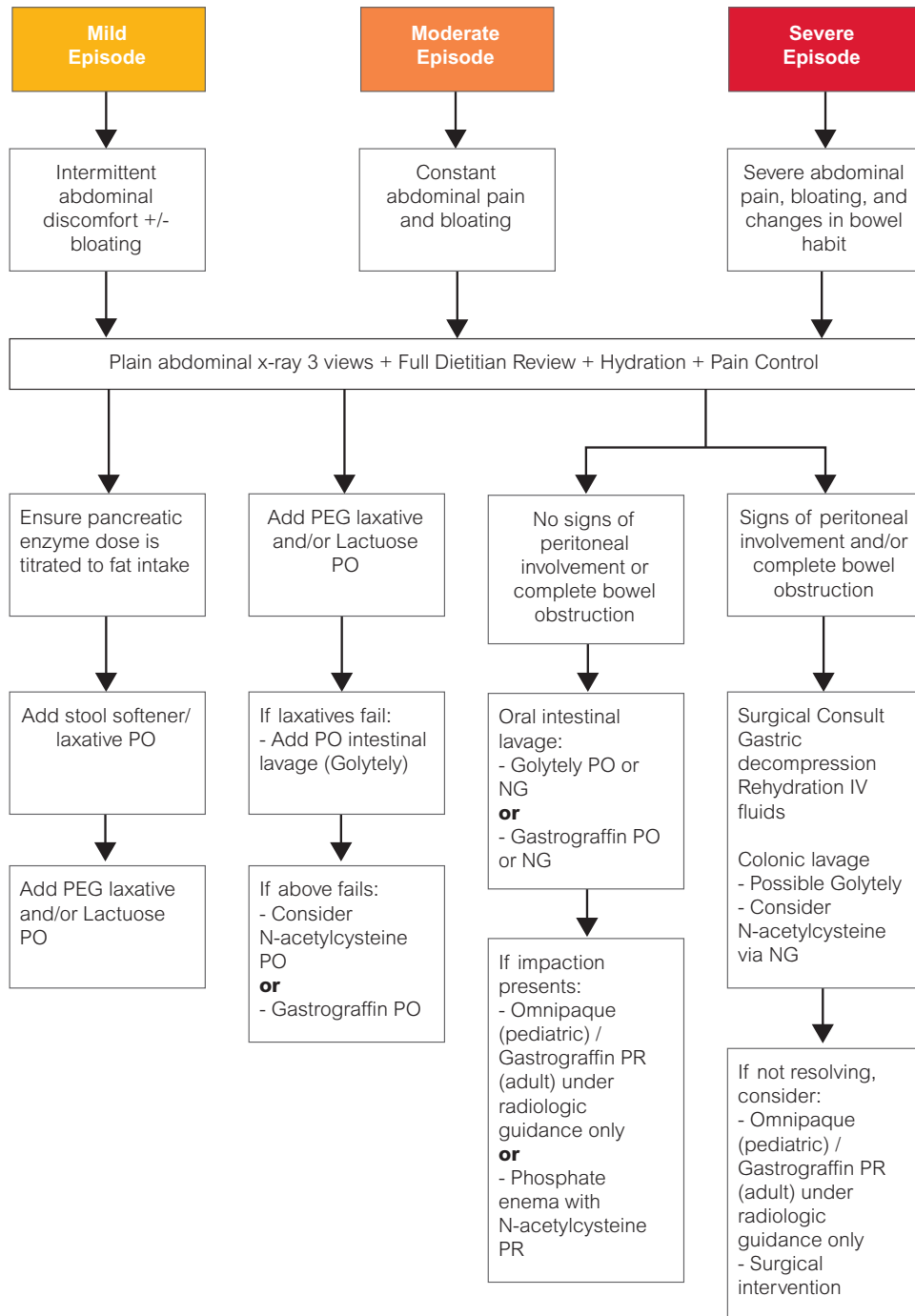
- Fibrosing colonopathy is a potential complication of high dose pancreatic enzyme replacement therapy.
- It was first described by Smyth et al. in 1994^{11, 12} in a series of patients with a presentation similar to DIOS but failure of resolution with conservative management. Dense strictures were found at surgery with diagnosis made by histopathological findings of submucosal fibrosis and bowel wall thickening.

Other causes of abdominal pain

- Consider other causes such as pancreatitis, biliary colic, cholecystitis, renal colic, among others.

Appendix

Figure 1:
Algorithm for the Treatment of Distal Intestinal Obstruction Syndrome



Endnotes

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