Treatment of Distal Intestinal Obstruction Syndrome


Introduction

The distal intestinal obstruction syndrome (DIOS), previously known as meconium ileus equivalent (MIE), is a condition unique to cystic fibrosis (CF). The syndrome is relatively common, occurring in about 10-22% of patients (Rubinstein et al, 1986; Penketh et al, 1987; Davidson et al, 1987; Dray et al, 2004). It may present at any time after the neonatal period but the incidence increases with age and it is more common in adolescent and adult patients. About 80% of cases present for the first time in adults. The recurrence rate is approximately 50%. Treatment of distal intestinal obstruction syndrome is easily misdiagnosed by those who are not familiar with the condition. It has not been described in other forms of pancreatic insufficiency but it has been reported in patients with cystic fibrosis who are pancreatic sufficient and have normal fat absorption (Davidson et al, 1987; Millar-Jones et al, 1995).

The pathogenesis of DIOS is partly due to loss of CFTR function in the intestine where it regulates chloride secretion from the crypts, bicarbonate secretion from Brunner’s glands and sodium transport. Intestinal obstruction has been reported as a major cause of mortality in CF mice with severe CFTR mutations (Walker et al, 2006). In addition to defective chloride secretion, CFTR regulates EnaC, NHE3 and anion exchangers leading to excess absorption and reduced secretion of fluid, which contributes to bowel obstruction. The incidence of DIOS is significantly greater in patients with severe genotypes. Patients who develop DIOS have significantly lower pulmonary function and a more rapid, but non significant rate of decline in lung function (Dray et al, 2004). This may be unrelated to DIOS and a confounding effect of age, severity of genotype and the presence of pancreatic insufficiency.

Physiological changes in the CF gut lead to the accumulation of viscous (sticky) mucus and faecal material in the terminal ileum, caecum and ascending colon which form obstructing mucofaeculant impactions (Walker et al, 2006). Contributing factors include fat malabsorption, abnormal intestinal mucins, low duodenal pH, deficient anion secretion, dysregulation of sodium and chloride absorption, defective bile acid uptake from terminal ileum, dysmotility (possibly a prolonged orocaecal transit time), dehydration with inspissated secretions especially in hot weather (Mascarenhas, 2003), previous laparotomy, and anticholinergic drugs (Andersen et al, 1990; Eggermont, 1996; Wilschanski & Durie, 1998). Dehydration associated with the development of diabetes mellitus (Hodson et al, 1976) or poorly controlled diabetes may also precipitate DIOS. Neonatal meconium ileus may predispose to DIOS (Escobar et al, 2005).

It has been suggested that a low dietary fibre intake might contribute to DIOS. However, despite the fact that people with CF have only half the fibre intake of non CF age matched controls (Gavin et al, 1997), colonic stool weight and stool bacterial load are greater in people with CF (Gavin, 2000). Increasing the dietary fibre intake to 18g per day appears to have little impact on the development of DIOS, as the maldigested and/or malabsorbed substrate and mucus assume the role of dietary fibre (Gavin, 2000).

Treatment of distal intestinal obstruction syndrome should be clearly differentiated from constipation and other gastrointestinal presentations. In classical constipation, the cause tends to be a low dietary fibre intake passing through the colon resulting in small pellets of stool (Cummings, 1986). However, in CF the most common cause of constipation is poorly controlled malabsorption and maldigestion. This results in large quantities of undigested substrate and mucus in the colon (Gavin, 2000), reducing peristalsis and increasing dysmotility. As the cause of CF constipation differs from classical constipation increasing dietary fibre intake will not have a significant beneficial impact on the CF colon and bulking agents will only further increase the substrate load.

Transplantation and DIOS

Distal intestinal obstruction syndrome is a well recognised complication in both children (Minkes et al, 1999) and adults (Gilljam et al, 2003), in the early post transplant period. It occurs with increasing frequency due to dehydration, immobility and bed rest, poor oral intake, drug therapy including high
dose opiates and post operative adynamic ileus.

Effective preventative measures and early treatment including the early introduction of enteral tube feeds, immediate introduction of pancreatin (even in the fasted patient) and the continuous administration of a GI lavage solution (if the patient is fasted for more than 24 hours) are important if severe complications are to be avoided (Gilljam et al., 2003). In addition, some centres have introduced a preventive protocol prior to surgery. Patients take a polyethylene glycol lavage solution (GoLytely) when they are called to the hospital for transplantation (Boyle & Orens, 2003).

**Analgesia**

Dehydration and opiate analgesics can potentiate acute and chronic attacks of DIOS. Appropriate preventative measure such as good hydration and prophylactic laxative therapy should be considered.

**Clinical presentation**

Patients may have intermittent acute exacerbations or chronic symptoms (Zentler-Munro, 1987). Typically patients develop progressive symptoms of recurrent colicky abdominal pain, bloating, nausea and anorexia, and signs of partial or complete small bowel obstruction, with a tender mass in the right iliac fossa. In the chronic form, DIOS can present in a more indolent fashion with symptoms such as anorexia, colicky abdominal pain, abdominal distension, fatty stools and constipation.

**Investigations**

Investigation should include a plain abdominal X-ray, which typically shows faecal loading in the right iliac fossa (often granular or bubbly in appearance), dilatation of the ileum and an empty distal colon. Fluid levels and a variable degree of small bowel dilatation may be seen during acute attacks. An abdominal ultrasound may be helpful in identifying the obstructing mass, but cannot be relied upon to exclude other serious causes of pain and obstruction such as intussusception (Dik et al., 1995). Computed tomography may help to clarify the diagnosis. Features seen include dilated small bowel and proximal colon with or without intestinal wall swelling. The intestines are filled with homogenous (faeculant) masses and there is usually a varying degree of fluid levels in the small bowel (Nassenstain et al., 2005). Serum amylase and electrolytes should be checked. If the condition is recurrent or unresponsive to medical treatment, a contrast enema or colonoscopy should be performed.

**Differential diagnosis**

Distal intestinal obstruction syndrome may mimic or be mimicked by other conditions such as simple constipation (Rubinstein et al., 1986; Agrons GA et al., 1996), appendicitis (may be atypical in CF) (Sheilds et al., 1990; Coughlin et al. 1990), an appendix mass, ovarian cyst, fibrosing colonopathy (Smyth et al., 1994; Smyth et al., 1995), pancreatitis (Shwachman et al., 1975), inflammatory bowel disease (Lloyd-Still, 1990), volvulus, intussusception, (Holmes et al., 1991), bowel adhesions (e.g. previous surgery for meconium ileus) (Littlewood, 1995). and gastrointestinal malignancy.

**Acute management**

Surgical review is recommended if there are signs of peritoneal irritation or complete obstruction. The patient should be kept “nil by mouth” and managed with intravenous fluids and nasogastric aspiration (drip and suck). A small dose of pancreatic enzymes should be continued every three to four hours even if the patient is nil by mouth to avoid further obstruction.

All patients presenting with acute DIOS should be well hydrated, intravenously if necessary. Pain relief with non-opioid analgesia is recommended and an antiemetic is often given.

There are variable treatment options and preparations may be administered either orally or via nasogastric tube. These include:

- Patients with mild episodes of DIOS often respond to laxatives such as lactulose and senna, or high dose Movicol®.
• High dose oral Gastrografin®.

• In the more severe case, DIOS can be successfully treated using Gastrografin® directed into the lumen of the ascending colon by means of either an enema or colonoscopy (O’Halloran et al, 1986; Shidrawi et al, 2002).

• The intestines can be flushed out using a balanced electrolyte solution such as Klean-Prep®, which may need to be given via nasogastric tube. With the administration of a polyethylene glycol electrolyte solution and other treatments, a clear effluent may not be the endpoint of treatment and a plain abdominal X-ray should always be obtained to document any retained stool (Mascarenhas, 2003; Cleghorn et al, 1986; Koletzko et al, 1989).

• Oral N-acetylcysteine (Parvolex®) acts as a mucolytic and can help break up the protein matrix of the inspissate.

• In a few refractory cases surgical decompression may be required but there is a high post operative morbidity. In some cases, caecostomy with manual evacuation can be successful. A few patients may need a right hemicolectomy and small bowel resection.

• In cases of DIOS resistant to conventional therapy, a modified antegrade continence enema technique creating a continent stoma may prove an effective alternative to more conventional surgery (Clifton et al, 2004). The successful use of laparoscopic placement of a Chait caecostomy device via appendicostomy has been reported in three children who had refractory constipation secondary to CF with DIOS (Stanton et al, 2002).

**Chronic management**

A number of studies have suggested that DIOS occurs more frequently in patients on inadequate pancreatic enzyme replacement. Review by an experienced dietitian to ensure that pancreatic enzyme dose is titrated to fat intake and to encourage adherence to routine dietetic management is essential. Care should be taken when increasing pancreatic enzyme supplementation in patients with abdominal pain and constipation as it is likely to worsen their symptoms, unless fat malabsorption is confirmed (Littlewood, 1995). An increase in fluid intake should be recommended and a review of dietary fibre intake should be undertaken. However, it is not always appropriate to increase the dietary fibre intake as patients with CF may already suffer from large bulky stools. In addition, increasing dietary fibre intake may lead to a detrimental reduction in the energy density of the diet. Timing of enzyme therapy with respect to meals and snacks and method of taking pancreatic enzymes should also be reviewed. An experienced CF dietitian should undertake this review (Littlewood & Wolfe, 2000). Hydration of the patient and of the contents of the GI tract is also important, especially in hot weather and during exercise (Kreimer et al, 1999).

Faecal chymotrypsin is low in untreated pancreatic insufficient patients with CF and has in the past been useful for monitoring enzyme therapy with low values suggesting inadequate therapy possibly due to poor adherence (Littlewood & Wolfe, 2000).

In addition to assessment of enzyme therapy, assessment of malabsorption and/or steatorrhoea is valuable. The 72 hour faecal fat collection is the gold standard for assessing fat absorption but is becoming less common and less readily available. Faecal fat microscopy has been shown as a useful tool to detect steatorrhoea. Fat microscopy shows some correlation between microscopic grading and severity of steatorrhoea and has been validated by comparison with quantitative measurements (Walters et al, 1990). This test is also less readily available than in the past.

Reduction of gastric acid or acid suppression as a means of improving enzyme efficacy with a proton pump inhibitor has been reported and the addition of ranitidine, omeprazole or lansoprazole to reduce gastric acid secretion (Heijerman et al, 1993, Francisco et al, 2002; Proesmans et al, 2003) or taurine (Darling et al, 1985; Belli et al, 1987) may help to improve absorption.

Patients with mild episodes of DIOS often respond to laxatives such as lactulose (20 mls twice a day and senna). Some centres use sodium picosulphate or high dose Movicol (Norgine). Prolonged maintenance therapy with N-acetylcysteine (Celltech) can be used in patients with chronic DIOS.
(acetylcystein sachet 400 mg twice or three times a day or Parvolex liquid –children; 5-10 ml qds in orange juice. Adults; 30 ml tds with 120 ml water or orange juice). Alternatively some patients appear to respond to intermittent courses of either gastrografin (Schering), Fabrol or Klean Prep (Norgine) as long as it is administered with appropriate fluids.

**Post operative**

In the event of laparotomy and surgical decompression, it is recommend that a small dose of pancreatin is started even if patient is nil by mouth to avoid further obstruction. The principles of prevention and early treatment for DIOS used in the post transplant patient (see above) can be extended to all people with CF undergoing surgery that is likely to be followed by high dose opiates and post operative adynamic ileus (Boyle *et al*, 2003).

**Key points**

- Distal intestinal obstruction syndrome is a condition unique to CF. It occurs due to the accumulation of viscous mucus and faecal material in the terminal ileum, caecum and ascending colon

- The syndrome is relatively common, occurring in about 10-22% of patients

- It may present either acutely or chronically and can be easily misdiagnosed by those who are unaware of the condition

- Distal intestinal obstruction syndrome should be clearly differentiated from constipation and other gastrointestinal presentations

- Typically patients develop progressive symptoms of recurrent colicky abdominal pain, bloating, nausea and anorexia and signs of partial or complete small bowel obstruction

- Dehydration, transplantation and opiate analgesics can potentiate acute and chronic attacks of DIOS. Prophylactic measure should be instituted to avoid complications

- A specialist CF dietitian should be involved in the management of DIOS.

**References**


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Treatment of DIOS

Mild episodes
- Intermittent abdominal discomfort with or without bloating

Moderate episodes
- Intermittent abdominal pain and bloating

Severe episodes
- Severe abdominal pain accompanied by bloating and change in stool habit

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guidance

Plain abdominal film
- Review by an experienced dietitian to ensure that pancreatic enzyme dose is titrated to fat intake.
- Encourage regular adherence to treatment.

Treat with laxatives e.g
- Lactulose 20 ml bd (1-5 years 5 ml bd, 5-10 yr 10 ml bd)
- Senna 2 od (child >6 yr 1/2 adult dose)
- Alternatives
  - Sodium picosulphate 10 mg od (adult)
  - Movicol 1-2 sachets qds (dissolved in 125 ml of water) (adult)

Dietetic review
- Review by an experienced dietitian to ensure that pancreatic enzyme dose is titrated to fat intake.
- Encourage regular adherence to treatment.

- Lactulose 20 ml bd
- Senna 2 od
- (or alternative laxative)
- With
- Parvoles 30 ml tds Parvoles liquid—children: 5-10 ml qds in orange juice. (Adults: 30 ml tds with 120 ml water or orange juice or acetylcysteine sachet 400 mg bd or tds)

Hydration
- Review by an experienced dietitian to ensure that pancreatic enzyme dose is titrated to fat intake.
- Encourage regular adherence to treatment.
- If there are signs of peritoneal irritation or complete bowel obstruction a surgical review is indicated.

Surgical opinion
- Nil by mouth, intravenous fluids and nasogastric aspiration (drip and suck)
- Phosphate enema
- Parvoles via NG tube
- Children: 5-10 ml qds in orange juice.
- Adults: 30 ml tds with 120 ml water or orange juice.
+/- parvolex 30 ml tds Parvolex liquid
– children; 5-10 ml qds in orange juice.
Adults; 30 ml tds with 120 ml water or
orange juice) or acetylcystein sachet
400 mg bd or tds

If rectal impaction present give
phosphate enema with 50 mls parvolex
PR

In resistant cases consider
Gastrografin enema
or
Colonoscopy with
installation of gastrogafin