Abdominal Pain, Meconium Ileus, Constipation and Distal Intestinal Obstruction Syndrome (D.I.O.S):

There are many causes of abdominal pathology in patients with CF, including meconium ileus in infants and distal intestinal obstruction syndrome (D.I.O.S) in older children and adults. Doctors, particularly surgeons, with limited experience of CF may consider these causes and it is important that patients do not undergo surgery. It is important that DIOS is considered in patients presenting with constipation. Equally, causes other than D.I.O.S should be considered. All patients presenting with abdominal pain should be discussed with the CF team.

Differential diagnosis of abdominal pain in CF:

- Inadequate pancreatic enzyme replacement cause colicky abdominal pain with steatorrhoea. (Most common cause of abdominal pain but cause is usually recognised by patients.)
- D.I.O.S - abdominal pain, constipation and bloating, +/- vomiting, +/- mass in right iliac fossa.
- Appendicitis [1] (5%; the most common ‘non D.I.O.S’ cause. May present classically or cause chronic RIF pain. Disease is modified by antibiotics used to treat the chest. Thick walled, dilated appendix may be visible on an ultrasound.
- Reflux oesophagitis and gastric ulceration. (Hyperactivity and slowed gastric emptying.)
- Gall-bladder disease. (Gall stones occur in up to 20% of adults with CF patients, biliary colic is common, however cholecystitis can also occur.)
- Intussusception in younger patients with episodic bouts of severe colicky pain, palpable mass and vomiting. If detected on an ultrasound, refer to paediatric surgeon.
- Volvulus.
- Acute pancreatitis. (Occurs more frequently in pancreatic sufficient patients.)
- Inflammatory bowel disease.
- Fibrosing colonopathy. (Affect the descending colon. It is related to the excessive use of high strength pancreatic enzyme replacement products.)
- Splenic/hepatic capsular pain. (Cirrhosis rarely causes liver pain. Splenic infarcts may occur with portal hypertension; liver capsule pain with cor pulmonale.)
- Clostridium difficile infection. (Atypical, often without diarrhoea.)
- Urinary tract infection.
- Renal stones. (Occur in 6% of CF patients. Caused by bowel bacterium oxalobacter formigenes being killed by antibiotics. Oxalates form in the bowel. These are absorbed and then excreted by kidneys where they precipitate to form stones. Treatments include, rehydration, avoid vitamin C excess, dietary modification and lithotripsy.)
- Irritable bowel syndrome.
- Helicobacter pylori infection. (Less common than in non CF patients. 30% less likely, DF508 appears to be protective.)
- Other causes included but not limited to, gastroenteritis, adhesions, testicular torsion, gynaecological causes and narcotic drug with drawl.

Meconium ileus (M.I):

Meconium ileus is a clinical presentation of CF that occurs in approximately 15% of new cases. It may be associated with ileal atresia. M.I presents in a newborn with delayed passage of Meconium, abdominal distension, vomiting and intestinal obstruc-
tion. Radiological appearances are characteristic with ‘soap bubble’ appearance of bowel contents and dilated small bowel. Antenatal perforation can occur with intra-abdominal calcification and peritonitis. Patients should be managed in a paediatric surgical unit where conservative treatment with Gastrografin. A hyperosmolar contrast medium given as enemas and/or naso-gastric tube may be successful. Otherwise surgery will be required to remove the meconium plug, exclude ileal atresia and if necessary resect any non-viable bowel. The baby should be stabilised, with a naso-gastric tube, intravenous fluids (10% dextrose with electrolytes) and transferred to the regional paediatric surgical unit at the British Royal Hospital for Children.

**Distal Intestinal Obstruction Syndrome (D.I.O.S):**
Distal Intestinal Obstruction Syndrome occurs in older patients with cystic fibrosis and is much more likely to occur in those that are pancreatic insufficient (PI). There are reports of D.I.O.S in a small number of CF cases that are pancreatic sufficient (PS). [2][3]

Risk factors associated with CF include:
- Dehydration
- Rapid increase in enzyme dosage
- Viscid intestinal secretions
- Altered gut motility and pH
- Poor compliance with enzyme therapy.[4]

Therefore hot environments for example summer holidays, changes in enzyme medication - particularly poor compliance or conversely too large a dose taken in one bolus rather than distributed through the meal - may precipitate D.I.O.S. Altered gut motility and pH may relate to changes in gut flora, especially Clostridium difficile (C.Diff). [5] Crisps eaten without pancreatic supplements have also bee reported to have causes cases of D.I.O.S.[6]

Clinical Presentation of D.I.O.S in CF:
Usually the problem arises in older children and adults who present with abdominal pain, constipation and bloating. A mass may be palpable in the right iliac fossa. There may or may not also be vomiting. The differential diagnosis (above) is important and other possible causes need to be considered and where appropriate, excluded from the investigation.

**Investigations - Discuss with radiologist:**
- Plain abdominal radiology - may show a mass of faecal material, or dilated bowel.
- Erect chest X-ray - to exclude perforation.
- Stool sample for culture, virology, fat stain, H. pylori antigen and C. Diff toxin tests.
- Blood tests - Renal function and electrolytes, amylase, liver function, WBC, glucose, inflammatory markers and cultures.
- Urinalysis.

Then as clinically appropriate:
- Abdominal ultrasound - to detail abdominal anatomy, free fluid, bowel thickening, appendix mass, intussusception, gallstones and evidence for portal hypertension etc.
- Barium/Gastrografin enema - by a specialist radiologist, this can
diagnose and help treatment at the same time.

- If diagnosis is still unclear, request a surgical opinion, however have a CT scan of the abdomen prior to considering a laparoscopy/otomy.

Treatment Options for D.I.O.S:
There are no RCT's for the outcome of treating episodes of DIOS. There are only isolated reports or series of small numbers of patients. Management is therefore at the consensus level and based on anecdotal evidence.

Acute/Sub-Acute:
- If vomiting, allow only clear fluids PO until discussed with the senior doctor.
- Avoid opiate analgesia.
- Continue with usual enzyme preparation, even if not eating, start with 2 capsules every 2 hours. Pancrex powder is available from pharmacy for patients who have a gastrostomy or NG tube and are unable to eat. A heaped teaspoon mixed with 50mls of sterile water every 2-4 hours is usually sufficient until they can resume their creon.
- Sign and symptoms of obstruction should be discussed with the surgical team.

Fluids and Hydration:
- Rehydration and maintenance of adequate fluid intake is essential. Give IV fluids especially if vomiting or dehydrated. Maintain an intravenous route if Gastrografin is to be used. Saline 0.9% is recommended for initial rehydration but continual care must be taken to avoid sodium overload. Potassium supplements will be needed according to electrolyte monitoring.

The following are possible treatment options:
Gastrografin - Oral[7] - Do not give if a complete bowel obstruction is present:
- <10kg: 25ml in 75ml water or juice.
- 10kg - 25kg: 50ml in 150ml of water or juice.
- >25kg: 100ml in 200ml water of juice.

To be used for inpatients only because of fluid implications. The dose can be repeated daily but if symptoms worsen or complete obstruction ensues, seek surgical opinion. Follow up a therapeutic response (symptom relief a loose stool) with a daily dose of lactose to maintain a soft stool for at least a month and adjust the dose as an out patient.

Gastrografin - Rectal - Can be used if oral Gastrografin has failed or causes vomiting:
The patient must be receiving intravenous fluid for a Gastrografin enema as this is a hyperosmolar and neat Gastrografin will attract approximately 12 times its volume of fluid. This must be done with the support of the radiologist and administer under radiological guidance. Plane abdominal X-ray will be required 1 hour after the enema. Caution if there is colonic dilation, discuss with surgeons. This will also help to screen for features of a fibroitic colon or strictures due to fibrosing colonopathy, or other pathology.[8]
Dose as oral, however, dilute to 5 times volume with water for less than 5 years old and 4 times volume with water for those over 5 years old. IV maintenance fluids should always be ran concurrently.

Ethylene Glycol - Movicol or Klean Prep:
- Admit the patient.
- Aim is to take the solution until watery stool is passed PR and symptoms resolve.
- NG tube often required to administer sufficient amount
- Regular Movicol or Lactulose will be required once relief achieved.
- Stop if symptoms worsen, discuss with the the surgical team.

Movicol:
This has become popular as a means of disimpaction in constipation. It can be used in quite large dosage safely, even in the young. It is essential to be sure of the diagnosis and to ensure the patient takes adequate oral fluid. There are no published studies on the comparative efficacy to other agents such as Gastrografin. It is best used for patients with radiological loading of the distal colon. Escalate the dose according to size of patient:
- Up to 20kgs - start at 4 sachets of Movicol Paediatric Plain on a daily basis. Increase after 48 hours to maximum of 6 sachets. Each sachet should be mixed with 65ml of water or juice - i.e.. 260ml for 4 sachets.
- Over 20kgs - start at 6 sachets of Movicol Paediatric Plain on a daily basis and increase by 2 sachets after 48 hours to 8 sachets.
- For adults - 6-8 sachets of Movicol in 1litre of water on a daily basis for up to 3 days.

Maintain until clearance and symptom relief, then decrease to 1-4 sachets or Lactulose as a daily maintenance.

Klean Prep:
- Do not give with complete obstruction or bile stained vomit.
- Add contents of 1 sachet to 1 litre of water.
- Can be drunk or given via NG tube.
- Give earlier in the day, not at bedtime to avoid aspiration.
- Start at 10ml/kg/hr increasing to 25ml/kg/hr in increments as tolerated - given in aliquots.
- Maximum volume given is 100ml/kg or 4 litres - which ever is smaller - over 4 hours.
- After 4 hours, a review, including assessment of abdomen and circulation is required before delivering a repeat treatment over the next 4 hours - maximum daily dose is 200ml/kg or 8 litres.
- In those patients with diabetes or impaired glucose tolerance, hypoglycaemia is a risk and blood glucose should be monitored.

N Acetyl Cysteine - Parvolex:
This tastes and smells foul - rotting eggs. Probably best given through a NG tube. There are no published trials on it efficacy. When diluted with squash it is drinkable. Dosage is 10ml - 30ml of the intravenous 20% solution diluted in 40 - 120ml of water. Give every 8 hours. After
implementation, if there is no improvement after 24 hours, reconsider
diagnosis, discuss with a CF consultant regarding further investigation and
referral to surgeons.

Chronic Symptoms of D.I.O.S:

General considerations about improving patient digestion:
- Ensure up to date assessment by a CF dietician. Check compliance
  with enzyme supplements, dose, timing of intake, always with
  snacks and how they are taken - open or swallowed whole. An extra
dose at the end of a meal may help in those with delayed gastric
emptying. Pancreatic enzymes are made inactive by heat, for
example in a car glove box in the summer.
- Ensure adequate dietary roughage.
- In children. consider toilet routine (abnormal behaviours) - may
  require positive reinforcement star charts and psychological input.
- Consider prescribing laxatives - see below.
- Consider doing an estimation of stool fat - 3 day collection or
  semi-quantitative stool fat stain.
- Check for undiagnosed liver disease - Ursodeoxycholic acid may
  improve the fat absorption.
- Exclude coeliac disease - Blood for TTG.

If no progress is made, consider the following, which may improve the efficacy
of the pancreatic enzymes:
- Ranitide: 2mg - 4mg/kg twice daily - maximum 150mg bd in adults
- Omeprazole: 0.4mg - 0.7mg/kg twice daily - maximum dose 40mg
  bd in adults.
- Prokinetic Agents - Marcolide antibiotics, Domperidone etc.

Movicol:
- 1 - 6 years: Movicol Paediatric Plain. 1 - 4 sachets daily, each in a
  cup of water or juice.
- 7 - 12 years: Movicol Paediatric Plain. 2 - 4 sachets daily, each with
  a cup of water or juice.
- >13 years: 1 - 3 sachets of Movicol daily, with 125ml of water per
  sachet.

Lactulose:
- 1 - 5 years - 5ml twice daily.
- 5 - 10 years - 10ml twice daily.
- 10 years - 15ml - 20ml twice daily.

This is used in mild and chronic cases. It probably treats constipation
rather than developed DIOS.

Fabrol Sachets - Acetyl Cysteine:
- 2 - 4 sachets given orally per day.
- Consider intermittent use of Gastrografin

**Constipation:**

- Simple constipation maybe difficult to distinguish from early D.I.O.S.
- Symptoms maybe similar but usually milder. It is important to ensure that
  patients with constipation do not have D.I.O.S. The AXR should be able to tell
you if a patient has simple constipation - if there is faecal matter loading in the colon or rectum with no signs of obstruction.
- Assess compliance with pancreatic enzymes.
- Ensure the patient has seen a CF dietician.
- Check diet for adequate fibre and fluid intake.

Medication options:
- Lactulose:
  - As above, Remind patients about the risk of tooth decay.
- Movicol:
  - For maintenance as per chronic D.I.O.S regimen.
- Sodium Picosulphate liquid:
  - <4 years - 250mcgs/kg at bedtime.
  - 4 - 10 years - 2.5 - 5 mg at bedtime.
  - >10 years - 5 - 10mg at bedtime.

This liquid is quite pleasant tasting and therefore acceptable to most patients. However, antibiotics do reduce its efficacy.
- Senna
  - 2 - 6 years - 7.5mg (as syrup, granules or tablet) at bedtime.
  - 6 - 12 years - 7.5mg - 15mg daily.
  - >12 years - up to 30mg daily.
- Docusate Sodium:
  - 2 - 12 years - 12.5mg - 25mg tds.
  - >12 years - 100mg - 200mg bd/tds

Other considerations:
- Consider Gastrografin and Klean Prep is these fail.
- Avoid bulking agents e.g.. methyl cellulose due to risk of bolus formation in terminal ileum.
- Avoid opiate analgesia

References:
6, Potato crisps without pancreatic extract supplements: a potential cause of the


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