Bile Acid Malabsorption/Diarrhoea

Bile acids are synthesised in the liver and stored in the gallbladder. They are released into the small bowel, where they aid in the digestion of lipids. Normally, 95% of bile acids are reabsorbed in the terminal ileum and are recycled back to the liver via the enterohepatic circulation.

If there is a failure of re-absorption, excess bile acids escape into the colon where they stimulate electrolyte and water secretion. This causes bile acid malabsorption (BAM) leading to bile acid diarrhoea (BAD). BAD presents as chronic watery, non-bloody diarrhoea. [1] [2]

Aetiology

The conditions causing BAM can be classified according to the aetiology. [3]

- Type 1 - ileal dysfunction (secondary BAM):
  - Ileal Crohn's disease, ileal resection.
  - Results in failure to reabsorb bile acids in the distal ileum, leading to BA spillover into the colon.
- Type 2 - idiopathic bile acid malabsorption (IBAM), primary bile acid diarrhoea:
  - Unknown cause.
- Type 3 - other conditions:
  - Post-cholecystectomy, post-vagotomy, coeliac disease, bacterial overgrowth, pancreatic insufficiency (chronic pancreatitis and cystic fibrosis).
  - May involve alterations in small intestinal motility, bile acid cycling frequency or composition of ileal contents.
- A fourth category of BAM may result from excessive hepatic bile acid synthesis - eg, due to the oral hypoglycaemic drug, metformin. [4]

Epidemiology

BAD is usually seen in patients with ileal Crohn's disease or ileal resection. However 25-50% of patients with functional diarrhoea or diarrhoea-predominant irritable bowel syndrome (IBS-D) also have evidence of BAM. It is estimated that 1% of the population may have BAM. [4]

Presentation

- Bile acid malabsorption leads to chronic watery, non-bloody diarrhoea. Many patients present with symptoms suggestive of IBS.
- Idiopathic BAM (no obvious cause) occurs in both men and women, mostly between the ages of 30 and 70.
- There is often a long history of diarrhoea at the time of diagnosis, sometimes lasting longer than 10 years.
- The diarrhoea is continuous or intermittent; nocturnal diarrhoea can occur.
- Mean stool volumes are moderately increased (240-290 g/day) but can be up to 900 g/day. [3]

Investigations [1] [5] [6]

The general approach to the diagnosis of BAM as a cause of chronic diarrhoea is a trial of a bile acid binder (see 'Management', below). If the treatment results in reduction of diarrhoea, the response is seen as an indirect proof of BAM. However, BAM is a chronic condition and it is therefore important to establish the diagnosis, as it requires lifelong treatment. [3]

- A relatively simple and highly sensitive method of testing for BAM is the ^{75}selenium homocholic acid taurine (^{75}SeHCAT) test. Retention of radiolabelled bile acids of less than 10-15% after seven days is abnormal.
- Measurement of total stool bile acid can also be used to diagnose BAM but stool collections for 48 hours or longer are required to account for variations, which can be difficult in practice.
- Serum 7-alpha-hydroxy-4-cholesten-3-one (C4), an intermediary in bile acid synthesis:
    - Increased C4 levels represent a marker for increased bile acid synthesis and increased faecal bile acid loss.
    - The disadvantages are that it requires a fasting sample, and it can lead to false positive results in patients with liver disease, or in patients taking medication that alters bile acid synthesis, such as statins.
    - Direct comparisons between the ^{75}SeHCAT retention test and serum C4 show that low ^{75}SeHCAT values correlate more closely with altered bowel habit, suggesting it is the better method to use for detecting BAM.

Differential diagnosis

The main differential diagnoses of non-bloody chronic diarrhoea in adults include: [7]

- Food allergy.
- Sugar maldigestion.
- Coeliac disease.
- Microscopic/lymphocytic colitis.
- Small bowel bacterial overgrowth.

See also separate Chronic Diarrhoea, Gastrointestinal Malabsorption and Irritable Bowel Syndrome articles.

Management

The main treatment goal with type 2 idiopathic BAD is control of diarrhoea with a low fat diet and oral bile acid binders. A low fat diet has been shown to be effective in reducing bile acid diarrhoea. [8] These reduce free bile acids in the small bowel and prevent the secretory action of bile acids on the colonic mucosa. BAM in patients with active inflammation of the terminal ileum in Crohn's disease may improve with glucocorticoids to induce remission. The underlying cause should be sought and treated for patients with type 3 BAM but they may also require a bile acid binder. [3]

There are currently three bile acid binders available: colestyramine, colestipol, colesevelam. Colestyramine treatment is by far the most studied of these agents. [9]

Bile acid binders have been shown to be effective in the control of bile acid-induced diarrhoea. The standard dose for each sequestrant can be titrated up or down in the individual patient, depending upon response. Excessive doses may lead to overcompensation resulting in constipation. These drugs are not absorbed in the intestine and therefore have no systemic side-effects.

Colestyramine and colestipol are anion exchange resins and may reduce absorption and serum concentrations of other drugs, including digoxin, thiazide diuretics, beta-blockers and thyroid hormones. Vitamin absorption may also be impaired.

Colesevelam binds bile acids with a higher affinity than colestyramine or colestipol and one study found that colesevelam appeared to be effective in patients who had failed treatment with cholestyramine. [3]

Complications

BAM can have a significant impact on a patient's lifestyle. Increased frequency of bowel motions often dictates the day-to-day functioning, limiting the ability to travel or leave the house. [3]

Prognosis [10]

A substantial proportion of patients with IBS-D will respond to cholestyramine. One review found that clinical response correlated with BAM severity. The overall response to therapy with cholestyramine was 96% for severe BAM (SeHCAT <5% of baseline), 80% for moderate or severe BAM (SeHCAT <10%), and 70% for any degree of BAM (SeHCAT <15%). Adverse effects of cholestyramine include constipation, nausea, borborygmi, flatulence, bloating and abdominal pain.

A long-term follow-up (mean 99 months) of 14 patients with chronic diarrhoea found that seven of the 14 patients experienced resolution of symptoms and no longer required cholestyramine. Of the remaining seven symptomatic patients, diarrhoea was well controlled in five using cholestyramine and in two using antidiarrhoeal medications.

Further reading & references

- BAM Support UK
- BSM - Bile Salt Malabsorption

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