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Bile acid malabsorption

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Bile acid malabsorption, known also as **Bile acid diarrhea**, is a cause of several gut-related problems, the main one being chronic diarrhea. It has also been called Bile acid-induced diarrhea, Cholerheic or Choleretic enteropathy and Bile salt malabsorption. It can result from malabsorption secondary to gastro-intestinal disease, or be a primary disorder, associated with excessive bile acid production. Treatment with bile acid sequestrants is often effective.

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Classification [edit]

Bile acid malabsorption was first recognized in patients with ileal disease.[1] When other causes were recognized, and an idiopathic, primary form described,[2] a classification into three types was proposed:[3]

- Type 1: Bile acid malabsorption, secondary to ileal resection, or ileal inflammation (e.g. in Crohn's disease)
- Type 2: Idiopathic bile acid malabsorption, Primary bile acid diarrhea
- Type 3: Secondary to various gastrointestinal diseases including cholecystectomy, vagotomy, small intestinal bacterial overgrowth, radiation enteropathy, celiac disease, chronic pancreatitis, etc.

Mechanisms of disease [edit]

Enterohepatic circulation of bile salts [edit]

Bile acids (also called bile salts) are produced in the liver, secreted into the biliary system, stored in the gall-bladder and are released after meals stimulated by cholecystokinin. They are important for the digestion and absorption of fats (lipids) in the small intestine. Usually over 95% of the bile acids are absorbed in the terminal ileum and are taken up by the liver and resecreted. This enterohepatic circulation of bile acids takes place 4-6 times in 24 hours and usually less than 0.5g /24h of bile acids enter the large intestine. When larger amounts of bile acids enter the large intestine, they stimulate water secretion and intestinal motility in the colon, which causes symptoms of chronic diarrhea.

Intestinal absorption of bile acids [edit]

The ileum is very efficient at absorbing the glyco- and taurine-conjugated forms of the bile salts. The apical sodium-dependent bile salt transporter (ASBT, IBAT, gene symbol *SLC10A2*) is the first step in absorption at the brush-border membrane. The cytoplasmic ileal bile acid binding protein (IBABP, ILBP, gene symbol *FABP6*) and the basolateral heterodimer of OSTα and OSTβ transfer bile acids through and out of the cell where they eventually enter the portal vein. These bile acid transporters are all highly expressed in the ileum but not in the liver, jejunum or colon.[4] When expression of these specialized transporters is reduced, the intestine is less efficient at bile acid reabsorption (Type 1 bile acid malabsorption). If intestinal motility is affected by gastro-intestinal surgery, or bile acids are deconjugated by small intestinal bacterial overgrowth, absorption is less efficient (Type 3 bile acid malabsorption). A very small proportion of the patients with no obvious disease (Type 2 bile acid malabsorption) may have mutations in ASBT,[5] but this mutation is not more common in most patients and does not affect function.[6]

Overproduction of bile acids [edit]

Primary bile acid diarrhea (Type 2 bile acid "malabsorption") may be caused by an overproduction of bile acids.[7][8] Several groups of workers have failed to show any defect in ileal bile acid absorption in these patients, and they have an enlarged bile acid pool, rather than the reduced pool expected with malabsorption.[9] The synthesis of bile acids in the liver is negatively regulated by the ileal hormone fibroblast growth factor 19 (FGF19), and lower levels of this hormone result in overproduction of bile acids, which are more than the ileum can absorb.[8]

Diagnosis [edit]

Several methods have been developed to identify the disorder but there are difficulties with all of them.[10] Fecal bile acid quantification is unpleasant for both the patient and laboratory. Diagnosis of bile acid malabsorption is easily and reliably made by the SeHCAT test. This nuclear medicine

test involves two scans a week apart and so measures multiple cycles of bile acid excretion and reabsorption. There is limited radiation exposure (0.3mSv). Retention of SeHCAT at 7 days is normally above 15%; values less than 15%, 10% and 5% predict respectively mild, moderate and severe abnormal retention and an increasing likelihood of response to bile acid sequestrants.[11] This test is not licensed in the USA, and is underutilized even where it is available.[12][13] Older methods such as the ^{14}C-glycocholic breath test are no longer in routine clinical use.

Measurement of 7 alpha-hydroxy-4-cholesten-3-one, a bile acid precursor, in serum, shows the increased bile acid synthesis found in bile acid malabsorption.[14] This test is an alternative diagnostic means when available. Fasting blood FGF19 values may have value in the recognition of the disease and prediction of response.[15]

Prevalence [edit]

Bile acid malabsorption is common in Crohn's disease but not always recognised. Most patients with previous ileal resection and chronic diarrhea will have abnormal SeHCAT tests and can benefit from bile acid sequestrants.

Patients with primary bile acid diarrhea are frequently misdiagnosed as having the irritable bowel syndrome as clinicians fail to recognize the condition.[12] When SeHCAT testing is performed, the diagnosis of primary bile acid diarrhea is commonly made. In a review of 18 studies of the use of SeHCAT testing in diarrhea-predominant irritable bowel syndrome patients, 32% of 1223 patients had a SeHCAT 7-day retention of less than 10%, and 80% of these reported a response to cholestyramine, a bile acid sequestrant.[11]

Estimates of the population prevalence taken from this review [11] suggest that 1% of the adult population could have primary bile acid diarrhea (Type 2 bile acid malabsorption).

Treatment [edit]

Bile acid sequestrants are the main agents used to treat bile acid malabsorption.[16] Cholestyramine and colestipol, both in powder form, have been used for many years. Unfortunately many patients find them difficult to tolerate; although the diarrhea may improve, other symptoms such as pain and bloating may worsen. Colesevelam is a tablet and some patients tolerate this more easily.[17][18][19] A proof of concept study of the farnesoid X receptor agonist obeticholic acid has shown clinical and biochemical benefit.[20]

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V·T·E· **Diseases of the digestive system (primarily K20–K93, 530–579)** [show]

Categories: Diseases of intestines | Diarrhea | GI tract disorders